

The Relationship between the Severity of Obstructive Sleep Apnoea Hypopnoea Syndrome and the Craniofacial Morphology in Adults

by

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ABSTRACT

Obstructive Sleep Apnoea / Hypopnoea Syndrome (OSAHS) is a potentially life-threatening breathing disorder, caused by recurrent upper airway obstruction during sleep. OSAHS is associated with an increased risk of cardiovascular disease and stroke, and there is a strong suspicion that untreated sleep disordered breathing precipitates greater mortality (Marin et al., 2005).

OSAHS affects 4-7% of the general adult population (Casero et al., 1999). Owing to its prevalence, it is currently considered a major public health concern, with severe physical and social consequences if not properly treated (Casero et al., 1999; Barthel SW and Strome M, 1999).

These disorders affect mainly middle-aged patients that are professionally active and may generate high losses and absences from work (Pieters T and Rodenstein DO, 2001). Medical costs of OSAHS may be significantly reduced when effective diagnosis and treatment are performed early (Kapur et al., 1999). However, the increasing demand for apnoeic diagnosis has begun to place strain upon services based on overnight laboratory studies. This situation has been clearly reflected at the Edinburgh Sleep Clinic where new referrals for polysomnography testing were found to have increased ten fold between 1990 and 1996, (Whittle et al., 1997).

Evidence suggests that the discrepancy between demand and available resources is steadily widening. The development of alternative diagnostic methods would therefore appear to be a worthy goal, and indeed this subject has received a great deal of attention within the recent literature.

Differences in cranio-cervico-facial morphology in the OSAHS subjects as compared to their 'normal' counterparts has been a consistent finding and more recent investigations have aimed to prove the existence of a relationship between cranio-cervico-facial morphology and severity of the OSAHS condition. Evidence has been equivocal, and although a number have been suggested a correlation, none have yet converted this into a tool of clinical diagnostic significance.

In this present investigation, sixty five (65) lateral cephalometric radiographs of subjects who had been referred to Edinburgh Royal Infirmary Sleep Centre for polysomnographic testing were retrospectively selected at random. To determine the existence of any correlation between the cranio-cervico-facial morphology and OSAHS severity as measured by the Apnoea Hypopnoea Index (AHI), a number of anatomic reference planes and points were used.

Statistically significant correlations were found when measuring angular and linear variables between the OSAHS subjects and the control group. Investigation of the angular and linear relationship between the measurements and the OSAHS severity, revealed significant results of clinical interest.

The findings thus provide evidence that subjects with obstructive sleep apnoea hypopnoea syndrome demonstrated significant alterations in cranio-cervico-facial form that may reduce the upper airway dimensions and subsequently impair upper airway stability and function.

DECLARATION

I do confirm that this work is entirely original and in no way taken from any external source except where a reference is cited.

.....

Adil Osman Mageet

July 10th, 2007

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LIST OF APPREVIATIONS

Symbol	Definition
OSAHS	Obstructive sleep apnoea / hypopnoea syndrome
AHI	Apnoea hypopnoea index
MSLT	Multiple sleep latency test
MRI	Magnetic resonance imaging
CSA	Central sleep apnoea
MSA	Mixed sleep apnoea
SRBD	Sleep-related breathing disorders
CT	Computed Tomography
FRC	Functional residual capacity
CNS	Central nervous system
RAS	Reticular activating system
BP	Blood pressure
EMG	Electro-myography
REM	Rapid eye movement
NREM	Non rapid eye movement
AN	Alae Nasi
GG	Genioglossus
GH	Geniohyoid
SH	Sternohyoid
TH	Thyrohyoid

TP	Tensor Palatini
DIA	Diaphragm
RC	Ribcage
O ₂	Oxygen
<i>Sa</i> O ₂	Oxygen saturation
<i>Sp</i> O ₂	Oxygen desaturation
<i>Pa</i> ,O ₂	Arterial oxygen tension
CO ₂	Carbon dioxide
<i>Pa</i> ,CO ₂	Arterial carbon dioxide tension
<i>P</i> _{ET} , CO ₂	Pharyngeal end-tidal carbon dioxide tension
TOPA	Topical oropharyngeal anaesthesia
CNAP	Continuous negative airway pressure
CPAP	Continuous positive airway pressure
nCPAP	Nasal continuous positive airway pressure
EPAP	External positive airway pressure
CSA	Cross sectional area
EEG	Electro-encephalography
SWS	Slow wave sleep
RDC	Respiratory disturbance index
TMJ	Temporo-mandibular joint
EDS	Excessive daytime sleepiness
SSS	Stanford sleepiness scale
ESS	Epworth sleepiness scale

MWT	Maintenance of wakefulness test
VAS-T	Visual analogue scale for tiredness
VAS-P	Visual analogue scale for performance
ESRF	End-stage renal failure
RLS	Restless legs syndrome
CAPD	Continuous ambulatory peritoneal dialysis
BMI	Body mass index
Wt (kg)	Weight per kilograms
Ht ² (m)	Height square
CHD	Coronary heart disease
NC	Neck circumference
PPNC	Percentage of predicted neck circumference
MRA	Mandibular repositioning appliance
NMR	Nuclear magnetic resonance
EOG	Electro-oculography
SIGN	Scottish Intercollegiate Guidelines Network
COPD	Coronary obstructive pulmonary disease
SpO ₂	Absorption of light by oxygenated and deoxygenated haemoglobin in blood
RCT	Randomized clinical trial
TRD	Tongue retaining device
TLD	Tongue locking device
TOPS	Tepper oral proprioceptive stimulator

TPE	Tongue positioner and exerciser
NAPA	Nocturnal airway patency appliance
SNOAR	Sleep and nocturnal obstructive apnoea reducer
MAA	Mandibular advancement appliances
ASPL	Adjustable soft palate lifter
IOD	Intra-oral devices
UPPP	Uvulo-palato-pharyngoplasty
LAUP	Laser assisted uvuloplasty
UPPGP	Uvulo-palato-pharyngo-glossoplasty
MSE-P	Minor symptoms evaluation-profile
RLS	Restless legs syndrome
PSG	Polysomnography
CCE	Cranio-cervical extension

INTRODUCTION

It is said that in 1843 John Wesley Hardin, the infamous Wild West gunfighter from Texas, shot and killed a loud snorer sleeping in the next room in a hotel in Abilene. He just could not put up with the noise any longer.

Dement WC, (1988) quotes a wise twentieth century physician who once said: “The practice of medicine ends when the patient falls asleep”. His intention was to highlight the disenfranchisement of the sleeping patient, which grew from the attitude that sleep represented a boundary that physicians may not cross. He describes the ‘prehistoric’ phase in understanding of sleep apnoea as existing prior to 1952, acknowledging apparently indiscriminate references to the condition during this period.

His colleague, Guilleminault C, (1985) observes that sleep apnoea syndrome provides an excellent example of what he describes as ‘syndrome rediscovery’ by astute clinicians in the twentieth century. With each, the new description of the ‘discovered’ syndrome is refined and the acknowledgement of the underlying pathophysiology has grown.

Obstructive Sleep Apnoea / Hypopnoea Syndrome (OSAHS) is a life threatening breathing disorder characterized by repeated collapse of the upper airway during sleep, with cessation of breathing. Patients with OSAHS are at risk of severe cardio-vascular and hypercapnia in addition to an overall reduced quality of life for sufferers and their families.

The aetiology appears to be a blend of anatomical and pathophysiological features. During sleep, the combination of a reduction in lingual and pharyngeal

muscle tone, alterations in breathing control, the supine position and reduced pharyngeal space may lead to airway occlusion in susceptible patients.

“...it is time for the nation to wake up to the staggering impact of (sleep apnoea) on the health and welfare of our society, an impact that rivals that of smoking” (Phillipson EA, 1993).

With increasing realization of prevalence and hence demand for treatment (Stradling JR, Crosby JH, 1991; Gleadhill et al., 1991; Young et al., 1993), perhaps the most significant rate limiting factor for the provision of treatment involves accurate diagnosis. The development of ‘Polysomnography’ in 1972, and later the ‘Multiple Sleep Latency Test (MSLT)’ (Carskadon et al., 1986 and 1987) has provided the scientific standard for diagnosis (Dement WC and Bilwise NG, 1988).

Diagnostic methods are also available to determine pharyngeal morphology in OSAHS patients: Lateral cephalometric radiographs, acoustic reflection, fluoroscopy, endoscopic observation, and computed tomography. Magnetic resonance imaging (MRI) is an innovative technique that produces high-resolution images without the use of ionizing radiation, making it especially well suited for soft tissue studies and diagnosis. Lateral cephalometric radiographs have been used by several investigators in an attempt to identify morphological parameters that might be characteristic of OSAHS.

The cranial base may be short (Bacon et al., 1988) and the cranial base angle reduced (Jamieson et al., 1986). Battagel JM, (1996) reported that cranial base angle (Ba-S-N) was significantly smaller 3.7° in OSAHS subjects and the length of the anterior cranial base reduced 2.4mm. This indicates a shortening of the antero-posterior dimension of the cranium and thus a more retruded face.

Rivlin et al., (1984), reported decrease in mandibular body length. Battagel JM, (1996) found reduced mandibular body length (Go-Me) by 5.9mm in the OSAHS group ($P=0.002$). Recording this distance in the horizontal plane, to take into account variations in mandibular plane inclination, the same differences were found. Gonion to menton was 6.6mm shorter and Gonion to point B was 5.6mm less in apnoeic individuals.

Bimaxillary retrusion (Lowe et al., 1986a; De Berry-Borowiecki et al., 1988) or retrognathia of the mandible alone have been reported (Jamieson et al., 1986; Tsuchiya et al., 1992). Battagel JM, (1996) found that intermaxillary space length- the distance between the posterior pharyngeal wall and the lingual aspect of the lower incisor at the level of the occlusal plane- was 5.7mm shorter in OSAHS subjects ($P=0.001$). The intermaxillary space area was reduced by 4.1cm^2 , indicating a lack of vertical compensation for the diminished antero- posterior development.

Treatment involves non-surgical and surgical techniques:

The non-surgical techniques include: elimination of the aggravating factors, weight reduction, training, pharmacological therapy, electrical stimulation of the upper airway, ENT assessment plus any necessary treatment, continuous positive airway pressure, intra-oral mandibular advancement appliances and nasal-valve dilator.

The surgical techniques include: tracheostomy, nasal surgery, pharyngeal surgery (uvulopalatopharyngoplasty), maxillofacial surgery, tonsillectomy, adenoidectomy, tongue reduction and bariatric surgery.

LITERATURE REVIEW

2.1 DEFINITION

Sleep apnoea syndrome was first described as early as 360 BC (Aelianus, 1666) and highlighted as 'Pickwickian Syndrome' (Dickens, 1836; Osler W, 1901). Reintroduced into modern medicine some decades ago (Spitz H, 1937; Burwell et al., 1956; Gastaut et al., 1966) the syndrome in recent years received copious attention in the medical literature. The term "apnoea" is derived from the Greek word "apnoia" meaning, "want of breath".

Sleep apnoea may be described as a potentially life-threatening breathing disorder in which periods of cessation of breathing (apnoeas) occur in the presence of inspiratory effort (Guilleminault et al., 1978; Douglas et al., 1982; Lowe et al., 1986a; Deegan et al., 1995; Battagel et al., 1996).

Three types of sleep apnoeas are reported by Gastaut et al., (1966): -

- Central sleep apnoea.
- Obstructive sleep apnoea hypopnoea syndrome (*occlusive or peripheral*).
- Mixed sleep apnoea.

2.1.1 Central Sleep Apnoea (CSA)

Central sleep apnoea (CSA) is defined as the cessation of both airflow and breathing effort and it is usually the result of neurological disorders. The condition can occur without identifiable causes; fortunately its occurrence is rare. Most sufferers have intermittent obstructive episodes. When more than 50% of events are central in nature, the form of the condition is defined as central.

Central sleep apnoea (CSA) is mainly due to an instability of the breathing control system, and its causes include alveolar hypoventilation disorders, heart failure, neurologic autonomic disorders and idiopathic forms of central sleep apnoea (Wisskirchen T and Teschler H, 2000). Patients with idiopathic CSA often complain of insomnia and awakening during sleep but may also suffer from daytime sleepiness. Cheyne-Stokes-Respiration or periodic breathing is often associated with heart failure and neurological disorders especially those involving the brain stem.

2.1.2 Obstructive Sleep Apnoea / Hypopnoea Syndrome (OSAHS)

Obstructive sleep apnoea / hypopnoea syndrome (OSAHS) is defined by the occurrence of five or more abnormal respiratory events per hour; these abnormal events include *apnoeas* (breaks in respiration for at least 10 seconds) and *hypopnoeas* (reduction in tidal volume accompanied by a 4% or greater fall in blood oxygen saturation, lasting more than 10 seconds), (Guilleminault et al., 1978).

Tangugsorn V, (1995) has defined obstructive sleep apnoea / hypopnoea syndrome as repetitive cessation of breathing, at the level of the nostrils and mouth lasting for at least 10 seconds, and occurring 30 times or more during 7 hours of nocturnal sleep in both rapid eye movement (REM) stage and especially in non-rapid eye movement (NREM) stage.

Obstructive sleep apnoea hypopnoea syndrome is also known as occlusive apnoea which is characterized by cessation of airflow because of upper airway obstruction despite simultaneous respiratory effort. This respiratory effort continues despite obstruction until the individual is aroused from sleep.

If the number of apnoeas / hypopnoeas exceeds 20 per hour, the condition is regarded as clinically significant (Riley et al., 1987). The Apnoea Hypopnoea Index (AHI) calculates the number of apnoea and hypopnoea divided by the hours of sleep, with a figure of “between” 5 to 10 being the upper end of normal (He et al., 1988).

The Scottish Intercollegiate Guidelines Network (SIGN) report (2003) on OSAHS has defined:

Apnoea - a ten second breathing pause.

Hypopnoea - a ten second event where there is continued breathing but ventilation is reduced by at least 50% from the previous baseline during sleep.

Obstructive sleep apnoea / hypopnoea syndrome (OSAHS) - the coexistence of excessive daytime sleepiness with irregular breathing at night.

Apnoea / hypopnoea index (AHI) - the frequency of apnoeas and hypopnoeas hourly (used to assess the severity of OSAHS).

Severity of OSAHS - (may be subdivided into varying degrees of breathing abnormality, depending on the AHI):

- Mild – (AHI 5-14/hr).
- Moderate – (AHI 15-30/hr).
- Severe – (AHI > 30/hr).

2.1.3 Mixed Sleep Apnoea (MSA)

Mixed sleep apnoea is described as a period of central apnoea followed by an obstructive apnoeic episode and is seen in around 5% of cases (Guilleminault C, 1976); it combines both obstructive and central apnoeas. The most common and

serious disorder in terms of morbidity and mortality is claimed to be obstructive sleep apnoea / hypopnoea syndrome (Phillipson EA, 1993).

2.2 PREVALENCE

Estimates of the prevalence of OSAHS depend on the age, sex of subjects studied as well as the definition and the method of diagnosis. OSAHS has a suggested prevalence of 2% in the general population (Shapiro CM, Dement WC, 1993). OSAHS is more prevalent in middle-aged overweight men and has a lower incidence in women (Kaplan R, 1990).

However the results of the most recent and comprehensive study suggest that 4% of middle-aged men (30-60 years) and 2% of middle-aged women have obstructive sleep apnoea hypopnoea syndrome (Young et al., 1993).

It is estimated that as many as 70% of adults with obstructive sleep apnoea hypopnoea syndrome (OSAHS) snored during childhood (Guilleminault et al., 1978; Koskenvuo et al., 1985; Hoffstein V, Mateika S, 1994; Ulfberg et al., 1996; and Young et al., 1996).

This high prevalence together with claims of wide ranging medical sequelae have led to the suggestion that sleep apnoea may be as significant a public health hazard as smoking (Phillipson 1993).

Prevalence rates may vary between different populations according to factors such as the prevalence of obesity. Age is also important and prevalence rates from 20% to 60% have been reported in the elderly (Ancoli-Israel 1994).

Epidemiological studies of habitual snoring in children suggest prevalence between 7% and 12% (Ali et al., 1993 and 1994). Children who snore are reportedly mouth breathers (McDonald JP, 1995; Carroll et al., 1995) or restless

sleepers, have excessive daytime sleepiness, are hyperactive, (Ali et al., 1993 and 1994), have poor hearing (Owen et al., 1996) and present with bilateral dental maxillary crossbite (McDonald JP, 1995). Although snoring has been reported to be a common finding in children only a subgroup of habitually snoring children have OSAHS.

2.3 PATHOGENESIS

Apnoeas are caused by obstruction of the airway during sleep at the level of the soft palate and tongue. (Royal College of Physicians Working Party Report, 1993).

Three broad factors determine upper airway patency during sleep; upper airway muscle activity, neuromuscular coordination, the size relationship of the upper airway and surrounding tissues (Remmers JE, 1978; Lowe AA, 1990b). Contraction of the genioglossus muscle moves the base of the tongue ventrally. Since the position of the anterior wall of the pharynx is determined in part by the tongue, contraction of the genioglossus muscle enlarges the volume of the oropharynx. Neuromuscular coordination ensures that contraction of the upper airway dilating muscles precedes the inspiratory onset of diaphragmatic activity. This provides a stable and distal upper airway before the onset of negative intraluminal pressure during inspiratory effort. Abnormal size relationship between the upper airway and its surrounding skeletal and soft tissues predisposes to upper airway occlusion during sleep. When an individual is lying down and asleep, the dimensions of the airway are modified by both posture and muscle tone. This occurs whether OSAHS is present or not, but the effects are greater in this condition (Horner et al., 1989; Pae et al., 1994). Not only is the effective

airway smaller in OSAHS subjects, but the tissue may be inherently more collapsible (Gleadhill et al., 1991). The pattern of heavy snoring which leads to airway narrowing and arousals has been termed the upper airway resistance syndrome.

Precipitation of OSAHS during pregnancy

Kowall et al (1989) reported a case of severe obstructive sleep apnoea developing during pregnancy. A 27-year-old primigravida was well until the sixth month of pregnancy, when she developed loud snoring and excessive daytime sleepiness. Polysomnography was performed at 36 weeks' gestation and revealed severe obstructive sleep apnoea. The patient was treated successfully during pregnancy with nasal continuous positive airway pressure, but continued to suffer from moderate obstructive sleep apnoea after delivery. This case suggests that sleep apnoea may be either precipitated or exacerbated during pregnancy.

A case report of OSAHS during pregnancy suggests a possible association with both intrauterine growth retardation and pre-eclampsia (Lefcourt LA, Rodis JF, 1996).

Obstructive sleep apnoea / hypopnoea syndrome in children

Marcus CL and Loughlin GM (1996) reported that obstructive sleep apnoea / hypopnoea syndrome is a common cause of morbidity during childhood. Childhood obstructive sleep apnoea syndrome is usually secondary to adenotonsillar hypertrophy. Other risk factors include craniofacial anomalies, obesity, neuromuscular disease and compressed maxillary arch with consequent approximation of the lateral turbinates and nasal septum (McDonald JP, 1995). Symptoms include snoring and difficulty in breathing during sleep. Definitive

diagnosis is made by polysomnography. Normative polysomnographic parameters vary with age; thus, age-appropriate norms must be used. In contrast to adults, children often manifest a pattern of persistent partial airway obstruction during sleep, rather than cyclical, discrete obstructive apnoeas. Most children are cured by tonsillectomy and adenoidectomy (Guilleminault C, Pelayo R 1998), or rapid palatal expansion (McDonald JP, 1995). However, some children require further therapy, such as continuous positive airway pressure (Guilleminault C and Pelayo R, 1998).

Guilleminault C and Pelayo R, (1998) stated that there is a familial predisposition to sleep-disordered breathing. Nasal obstruction and mouth breathing influence facial growth, which may further lead to difficulty in breathing while asleep. Symptoms include an increase in total sleep time, non-specific behavioural difficulties, hyperactivity, irritability, bed-wetting and morning headaches (Guilleminault C and Pelayo R, 1998). Clinical signs include failure to thrive, increased respiratory effort with nasal flaring and suprasternal or intercostal retractions (Guilleminault C and Pelayo R, 1998). In addition, abnormal paradoxical inward motion of the chest may occur during sleep (Guilleminault C and Pelayo R, 1998). Excessive daytime sleepiness and obesity are not always present (Guilleminault C and Pelayo R, 1998). Untreated children may develop cardiovascular complications (Guilleminault C, Pelayo R, 1998). The condition is treatable with continuous or bilevel positive airway pressure , and may be cured with surgery (Guilleminault C and Pelayo R, 1998).

Sleep-related breathing disorders (SRBD) can occur at any age. Obstructive sleep apnoea, upper airway resistance syndrome and obstructive hypopnoea syndrome all lay on the pathological continuum of SRBD (Messner AH, Pelayo R, 2000).

These disorders can have a great impact on a child's quality of life and can progress to significant complications.

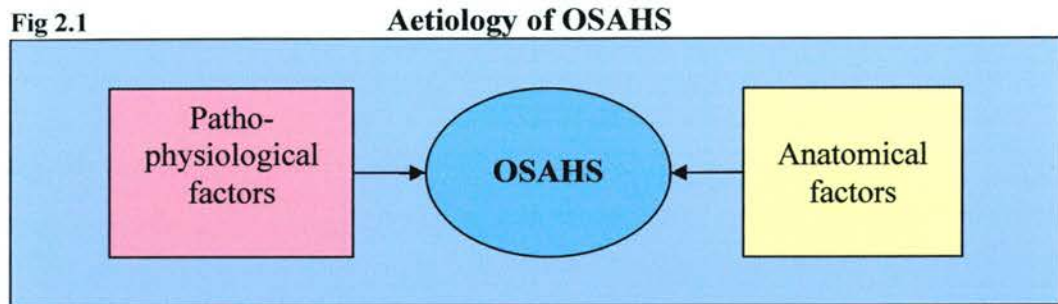
Adenotonsillectomy remains the mainstay of treatment. Nasal continuous positive airway pressure is effective and well tolerated in those who do not respond to adenotonsillectomy. In selected cases, additional surgery or supplemental oxygen (with careful monitoring) may play a role (Marcus CL, 1997), and in cases with compressed maxillary arches, rapid palatal expansion should be considered (McDonald JP, 1995).

Mogayzel et al., (1998) have studied sleep breathing disorders in 88 children with achondroplasia and concluded that:

- Children with achondroplasia often have sleep-related respiratory disturbances, primarily hypoxaemia.
- The majority do not have significant obstructive or central apnoea; however, a substantial minority are severely affected.
- Tonsillectomy and adenoidectomy decrease the degree of upper airway obstruction in most but not all children with achondroplasia and obstructive sleep apnoea.
- Restrictive lung disease can present at a young age in children with achondroplasia.

2.4 AETIOLOGY

The aetiology of OSAHS and the abnormalities that underlie the narrowing of the upper airway at the level of the pharynx is complex. OSAHS is thought to arise from a combination of pathophysiological and anatomical factors.



2.4.1 Pathophysiological Factors

Functional impairment of the muscles that dilate the upper airway is thought to be particularly important in the development of OSAHS and these patients demonstrate lower tonic and phasic contraction of these muscles during sleep than unaffected people (Deegan et al., 1995).

Table 2.1 Factors contributing to the pathophysiology of OSAHS

General factors	<ol style="list-style-type: none"> 1. Anthropometrics (sex, age and obesity). 2. Drugs (hypnotics and tranquillisers). 3. Genetics.
Reduced upper Airway calibre	<ol style="list-style-type: none"> 1. Specific anatomical lesions (enlarged tonsils and micrognathia). 2. Head position. 3. Nasal obstruction.
Mechanical factors	<ol style="list-style-type: none"> 1. Posture. 2. Upper airway resistance. 3. Upper airway compliance.
Upper airway muscle function	<ol style="list-style-type: none"> 1. Abnormal upper airway dilator muscle activity. 2. Impaired relationship of upper airway muscle and diaphragm contraction.
Upper airway reflexes	<ol style="list-style-type: none"> 1. Response to negative pressure. 2. Response to positive pressure. 3. Feedback from the lungs.
Central factors	<ol style="list-style-type: none"> 1. Chemical drive. 2. Periodicity of central drive. 3. Response to breath loading.
Arousal	<ol style="list-style-type: none"> 1. Impaired arousal responses. 2. Postapnoeic hyperventilation.

2.4.1.1 General factors

2.4.1.1.1 Sex.

Normal males have significantly higher pharyngeal and supraglottic resistance than normal females (White et al., 1985), which makes them more susceptible to pharyngeal collapse and OSAHS, and may contribute to the male predominance of the syndrome (Guilleminault et al., 1976). The mechanism underlying this higher upper airway resistance in males is unclear, but could be related to a possible protective effect of female sex hormones (Block et al., 1980), a possible deleterious effect of male sex hormones (Johnson et al., 1984), or to the greater incidence of obesity among males (White et al., 1985).

2.4.1.1.2 Age.

Pharyngeal resistance increases with age in normal men, possibly related to greater body weight (White et al., 1985), and it is widely believed that risk of developing OSAHS increases with age in men. However, this assumption is far from conclusive. One study has shown that, although there may be an increased incidence of sleep-disordered breathing among older (>50 years), when otherwise healthy subjects are compared to younger controls, the frequency of such sleep disordered events is not within the range of the OSAHS syndrome (Bixler et al., 1985). Another study demonstrated that 28% of randomly selected patients (>65 years) had apnoea frequencies of more than 5 episodes.h⁻¹, but many of these were asymptomatic, and it was suggested that an apnoea frequency in excess of 5 episodes.h⁻¹ may be a “normal” finding in this age group (Ancoli-Isreal et al., 1985).

2.4.1.1.3 Obesity.

It has long been recognized that there is an association between obesity and OSAHS (Walsh et al., 1972), and that weight loss can be very beneficial in the management of OSAHS (Harman et al., 1982, Suratt et al., 1987). One explanation for the relationship between obesity and OSAHS is that the upper airway is narrowed in obese patients as a result of increased fat deposition in the pharyngeal walls (Remmers et al., 1980). Studies using conventional computed tomography (CT) failed to identify any abnormal fat deposition in the immediate vicinity of the upper airway (Haponik et al., 1983; Suratt et al., 1983). However, the development of magnetic resonance imaging (MRI), which can make use of specially “weighted” images to detect fat, has led to the demonstration of increased fat deposition surrounding the collapsible segment of the pharynx in patients with OSAHS (Horner et al., 1989; Shelton et al., 1993).

The amount of fat detected also correlates with the subject’s apnoea / hypopnoea frequency (Shelton et al., 1993). Another possible explanation for the fact that obese subjects often have smaller lung volumes, particularly functional residual capacity (FRC), than non obese, which in turn indirectly influence upper airway size and contribute to upper airway narrowing (Hoffstein et al., 1984). The upper airway may also be narrowed in obese patients with OSAHS as a result of external compression by superficially located fat masses (Koeing et al., 1988; Koopman et al., 1981), and this could explain the finding that increased neck circumference correlates more closely than general obesity with the incidence and severity of OSAHS (Davies et al., 1990; Stradling et al., 1991).

In an experimental model, hard-filled bags, simulating cervical fat accumulation, were applied to the anterior neck of supine anaesthetised rabbits and were found

to increase upper airway resistance and decrease closing pressures (Koenig et al., 1988).

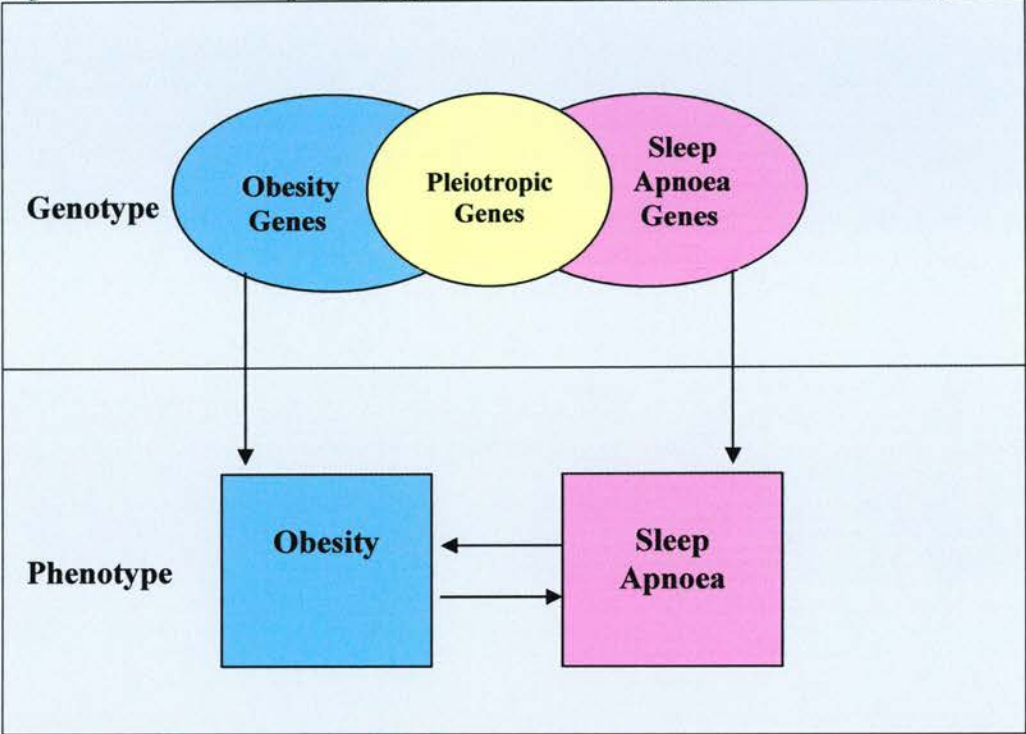
Genetics.

Ostructive sleep apnoea hypopnoea syndrome (OSAHS) is considered as a complex genetic disorder. Descriptive studies from several countries have consistently show familial aggregation of the apnoea hypopnoea index (AHI) and symptoms of OSAHS in both adults and children. Phenotypic markers of OSAHS have been identified, such as upper airway anomalies, abnormal breathing control, and obesity through which genes might act to increase susceptibility to OSAHS. The genetics of OSAHS may differ among racial groups. Two approaches have recently been used to investigate the genetics of OSAHS: a segregation analysis and a whole genome scan. Data suggested a common causal pathway regulating both OSAHS and obesity in Caucasian families (Gaultier C, 2003).

Patel SR, (2005) on his review article concluded that both obesity and sleep apnoea are heavily influenced by underlying genotype. Some susceptibility genes act directly on one phenotype and through the causal relationships between obesity and sleep apnoea have indirect effects on the other. Other loci have pleiotropic effects, impacting susceptibility to both obesity and sleep apnoea via independent mechanisms (Fig. 2.2). Sleep apnoea susceptibility genes may interact with obesity through numerous mechanisms to influence sleep apnoea predisposition. Genetic polymorphisms may modulate the degree to which obesity alters ventilatory drive, reduces lung volume, or narrows the upper airway. Other polymorphisms may affect the degree to which these stresses result in the

development of sleep apnoea. Similarly, obesity susceptibility genes may interact with sleep apnoea in its potential effect on obesity (Patel SR, 2005).

Fig 2.2 Shared susceptibility genes between sleep apnoea and obesity



2.4.1.1.5 Substances which depress the central nervous system.

Substances which depress the central nervous system (CNS), such as *alcohol*, *sedatives* and *tranquillizers* support relaxation of pharyngeal musculature and therefore airway occlusion (Battagel JM, 1996).

Alcohol.

Rossner et al., (1991) found high *alcohol* level in patients who had died of acute myocardial infarction, suggesting this may be an important factor contributing to OSAHS. Issa et al., (1982) found acute alcohol consumption promotes the development of apnoea during late sleep. Alcohol is a CNS depressant and as such will contribute to the hypotonicity of muscles with the pharynx, soft palate

and muscles of the tongue. Ethanol reduces genioglossus muscle activity during both quiet breathing and hypercapnia in healthy normal subjects. It is believed to have a depressant effect on the reticular activating system (RAS), and appears to have more profound effects on the upper airway muscles than on the ventilatory pump muscles (Kroll et al., 1984).

Hypnotics and tranquillizers.

Hypnotics and tranquillisers have an effect similar to that of alcohol. These agents promote relaxation of the pharyngeal musculature and therefore airway occlusion.

Diazepam is one of a group of medicines called benzodiazepine tranquillizers and are some instances used specifically for the relief of muscular spasm (British National Formulary 1998). Side effects of these drugs are to further relax any postural reflexes including those of muscles supporting the pharyngeal area.

Chloral hydrate and anaesthetics have a depressant effect on the reticular activating system (RAS), with hypnotic doses of chloral hydrate preferentially depressing genioglossus activity as compared with diazepam activity (Hershensen et al., 1984). This selective depression of upper airway muscle activity suggests that the respiratory activities of these muscles may be more dependant on the (RAS) than the bulbo-spinal phrenic system (Bonora et al., 1984).

Caffeine.

Bardwell et al., (2000) studied 61 subjects including normotensives and hypertensives with and without OSAHS: 38 men, 23 women, aged 30-60 y; 100-150% of ideal body weight; without other major illness. Patients were studied using polysomnography, caffeine consumption was assessed, 24-h urinary NE levels were examined and ambulatory blood pressure (BP) was recorded. Patients with OSAHS (N=27) reported significantly greater caffeine consumption than

those without OSAHS (N=34) (295 vs. 103 mg, $P=0.010$), but caffeine was not significantly correlated with their ambulatory BP. In contrast, NE excretion correlated with caffeine consumption ($r =0.24$, $P=0.041$), apnoea severity ($r =0.65$, $P <0.001$) and BP ($r =0.34$, $P <0.005$). Significant OSAHS-NE and BP-NE relationships remained even after controlling for caffeine consumption. Patients with OSAHS consumed nearly three times the amount of caffeine as patients without OSAHS. While caffeine partially explains the increased adrenergic tone in patients with OSAHS and the relationship between BP and NE, it does not appear to contribute significantly to the relationship between OSAHS and elevated BP.

2.4.1.2 Reduced upper airway calibre

2.4.1.2.1 Specific anatomical lesions.

Factors that reduce upper airway calibre lead to increased upper airway resistance, with the generation of a more negative pharyngeal pressure during inspiration (Lopes et al., 1983), and thereby predispose to upper airway occlusion during sleep. There are a number of recognised anatomical abnormalities that are associated with narrowing of the upper airway and predispose to OSAHS.

Specific anatomical abnormalities are more frequently seen in children, particularly adenotonsillar enlargement (Orr et al., 1981; Sussman et al., 1975). Conditions associated with facial dysmorphism and/or mandibular abnormalities show a predisposition to OSAHS, and include choanal atresia (Schafer et al., 1982), micrognathia (Schafer et al., 1982; Conway et al., 1977), and craniofacial dysostosis (Schafer et al., 1982; Lauritzen et al., 1986). Micrognathia is particularly associated with OSAHS, as a small and/or retropositioned mandible

places the base of the tongue closer to the posterior pharyngeal wall and interferes with the efficiency of the genioglossus muscle in keeping the tongue out of the narrowed pharynx (Sher et al., 1992). Surgical correction of specific anatomical abnormalities, such as adenotonsillar removal, can result in partial or complete resolution of OSAHS (Guilleminault et al., 1989).

Infiltration of upper airway muscles and soft tissues can impair muscle function and reduce the upper airway lumen, as in myxoedema (Orr et al., 1981), acromegaly (Grunstein et al., 1991), involvement by neoplastic processes (Zorick et al., 1980), and mucopolysaccharidosis (Perks et al., 1980), all of which have been associated with a predisposition to OSAHS. Treatment of the underlying process can reverse upper airway obstruction (Orr et al., 1981; Zorick et al., 1980). Most adult patients with OSAHS, however, have no specific skeletal or soft-tissue lesion obstructing the upper airway, but often have a small-congested oropharyngeal airway.

2.4.1.2.2 Head position.

The position of the head and neck is an important factor in pharyngeal patency, with neck flexion capable of producing considerable increases in pharyngeal resistance during wakefulness and anaesthesia, particularly in obese subjects (Safar et al., 1959; Spann et al., 1971). Varying head position between flexion and extension can cause significant variations in size of the retroglossal space and hyoid position on lateral cephalometry (Davies et al., 1990). Neck flexion makes the upper airway more susceptible to collapse, whilst neck extension makes the upper airway more resistant to collapse (Wilson et al., 1980), irrespective of changes in general body posture.

Mouth opening can cause increased upper airway resistance, since this results in dorsal movement of the ventral attachments of upper airway dilator muscles, with resultant shortening in muscle length and reduction in efficiency (Morikawa et al., 1981).

2.4.1.2.3 Nasal Obstruction.

In normal individual, the nose is the primary route of breathing during wakefulness, and more particularly during sleep (Gleeson et al., 1986), and the nose accounts for about half of the total respiratory resistance to airflow (Proctor et al., 1977). A marked increase in nasal resistance is seen in patients with acute or chronic rhinitis when they become recumbent (Rundcrantz H, 1969). Unilateral nasal disease, such as polyps, can also cause increased nasal resistance in the lateral recumbent position if present in the upper - most nostrils (Cole et al., 1984). Nasal resistance is elevated in OSAHS patients (Martin et al., 1980; Irvine et al., 1984), and the use of nasal decongestants can reduce supraglottic resistance in OSAHS (Anch et al., 1982). Nasal occlusion in normal subjects leads to increased numbers of apnoeic episodes, sleep arousals, and awakenings (Suratt et al., 1986), and increased numbers of apnoeas and hypopnoeas are also seen in patients with seasonal allergic rhinitis when symptomatic (McNicholas et al., 1982), or with deviated nasal septum (Lavie et al., 1982).

Nasal packing for epistaxis may induce OSAHS or exacerbate pre-existing OSAHS (Wetmore et al., 1988) whilst topical anaesthesia of the nose significantly increases the number of disordered breathing events in normal sleeping subjects (McNicholas et al., 1987; White et al., 1985).

The capacity to sense both pressure and airflow in the upper airway may be important in the maintenance of respiratory rhythm during sleep (Zwillich et al., 1981), and nasal airflow has been reported to have a stimulant effect on breathing (McNicholas et al., 1993). There is strong evidence, therefore, from a number of different perspectives, to support an important role for nasal dysfunction in the pathophysiology of OSAHS.

2.4.1.3 Mechanical factors

Fibrotic studies during obstructive sleep apnoea / hypopnoea syndrome have shown abrupt collapse of the airway at the onset of inspiration, with opposition of the lateroposterior oropharyngeal walls in the pharynx and no evidence of glottic obstruction (Guilleminault et al., 1978). On lateral fluoroscopy (Suratt et al., 1983), upper airway obstruction during inspiration is seen when the soft palate touches the posterior pharyngeal wall and the tongue. This obstruction usually ends when the tongue moves forward, the mandible lifts and the posterior pharyngeal wall moves posteriorly. This sequence of events enlarges the pharyngeal airway.

2.4.1.3.1 Posture.

Most individuals assume the supine posture when they are asleep, despite the disadvantageous effects that this posture has on upper airway patency. Pharyngeal cross sectional area is reduced from the upright to the supine position in normal subjects (Brown et al., 1987; Yildirim et al., 1991). Supraglottic resistance is also greater in the supine than in the sitting position, both for normal subjects and patients with OSAHS (Anch et al., 1982).

The effect of supine posture on upper airway patency does not result from decreased upper airway dilator muscle activity, since these muscles increase their electro-myographic (EMG) activity with the transition from the upright to the supine posture both in OSAHS and normal subjects (Safar et al., 1959; Yildirim et al., 1991; Douglas et al., 1993).

There is also no evidence that the decrease in lung volume observed in supine posture contributes to upper airway narrowing, since maintaining functional residual capacity (FRC) at a constant level in normal subjects whilst changing from upright to supine does not prevent the fall in cross sectional area (Rundcrantz H, 1969). Thus, the supine posture effect appears to be due to gravitational forces acting to narrow the upper airway (Rundcrantz H, 1969). However, patients with OSAHS often have a reduced FRC when upright, and the further fall in FRC when assuming the supine position may be associated with a significant fall in upper airway calibre (Hoffstein et al., 1984).

2.4.1.3.2 Upper airway resistance.

Patients with OSAHS have smaller upper airways than nonapnoeic subjects and this is reflected in the finding of a higher awake inspiratory airflow resistance during wakefulness within the nasopharynx, in OSAHS patients when compared to controls (Anch et al., 1982; Stauffer et al., 1987).

The onset of sleep leads to an increase in respiratory system resistance in healthy humans (Lopes et al., 1983; Hudgel et al., 1984; Tabachink et al., 1981; Weigand et al., 1989 and 1990; DeWeese EL, Sullivan TY, 1988), the increase being located almost entirely in the upper airway above the larynx (Hudgel et al., 1984),

primarily at either the level of the palate or oropharynx (Hudgel DW, Hendricks C, 1988).

Although the nose can contribute significantly to upper airway resistance on assuming the supine posture due to increased nasal mucosal congestion (Anch et al., 1982), there is little increase in nasal resistance with the change from wakefulness to sleep (Hudgel et al., 1988). The further increase in upper airway resistance with sleep onset is thought to result instead, from a decline in upper airway dilator muscle tone during sleep (Hudgel et al., 1988).

Non-obese snorers have a greater increase in total airway resistance during non-REM sleep than matched control subjects (Skatrud JB, Dempsey JA, 1985), and there is a highly significant correlation between awake nasopharyngeal resistance and AHI during sleep (Stauffer et al., 1987; Suratt et al., 1985). Inspiratory oropharyngeal resistance can reach high levels between apnoeas in patients with OSAHS (Remmers et al., 1978; Martin et al., 1980), and expiratory resistance increases significantly, as an apnoeic episode approaches (Sanders MH, Moore SE, 1983; Sanders et al., 1985).

2.4.1.3.3 Upper airway compliance and collapsibility.

The upper airway extends from the nasal choanae to the epiglottis in humans. It lacks rigid or bony support, and may thus collapse in the absence of forces to maintain patency (Hudgel DW, 1986).

Marked variability in upper airway collapsibility is seen among normal men during sleep (Wiegand et al., 1989), and is thought likely to be related to both anatomical factors and alterations in ventilatory control during sleep. Pharyngeal compliance in snorers with OSAHS is increased compared to nonapnoeic snorers

(Brown et al., 1985 and 1987), and patients with OSAHS have more collapsible upper airways whilst awake than control subjects (Suratt et al., 1984 and 1985).

Increased pharyngeal compliance may, therefore, be more closely related to the development of OSAHS than pharyngeal cross sectional area (Brown et al., 1985).

Patients with OSAHS have lower tonic muscle activity than snoring non-apnoeic controls, which appears to make their pharynx “floppier” (Brown et al., 1987).

This concept has been extended by viewing the upper airway as a Starling resistor, with a collapsible segment in the oropharynx and flow through the upper airway governed by changes in pressure occurring upstream (nose) rather than downstream (hypopharynx) to the collapsible segment (Smith et al., 1988; Schwartz et al., 1988). Patients with OSAHS may, therefore, have an elevation of the critical collapsing pressure surrounding the upper airway, rather than changes in the resistive properties of the upper airway (Smith et al., 1988; Schwartz et al., 1988).

Overall, the data points to important differences in upper airway mechanics between normal subjects and patients with OSAHS, which are evident during wakefulness, but become more during sleep.

2.4.1.4 Upper airway muscle function

2.4.1.4.1 Abnormal upper airway dilator muscle activity.

Patency of the collapsible segment of the upper airway is believed to be dependant on the function of pharyngeal dilator muscles (Remmers et al., 1978; Block et al., 1984), which act to stiffen or distend the collapsible pharyngeal airway during inspiration, as suggested by the presence of EMG activity

coordinated with respiration (Strohl KP, 1981). Activity of these upper airway muscles is modulated by chemical stimuli, vagal input, changes in upper airway pressure, and baroreceptor activity (Brouillette et al., 1979 and 1980).

Breathing through a narrowed upper airway generates a greater suction pressure and, thus, greater collapsing force, and pharyngeal dilator muscles must, therefore, contract more forcefully to prevent upper airway obstruction. Progressive hypercapnia, hypoxia, asphyxia and negative pressure application all produce an augmenting drive to upper airway dilator muscles (Brouillette et al., 1980; Horner et al., 1991). Defects in such upper airway muscle responses, or in coordination of upper airway and diaphragm activity, have each been proposed as factors predisposing to OSAHS (Wilson et al., 1980; Brouillette et al., 1980; Weiner et al., 1982; Onal et al., 1981 and 1982; Issa et al., 1983).

The alae nasi (AN) dilate the anterior nares during inspiration, and the degree of preactivation of the AN EMG ahead of the DIA EMG may be used as an index of ventilatory drive to the upper airway (Strohl et al., 1980). During NREM sleep, AN preactivation increases from the beginning to the end of an apnoeic episode suggesting that ventilatory drive to the AN increases with apnoeic duration (Suratt et al., 1985). This increase in preactivation, which also be seen in other upper airway muscles (Strohl et al., 1980), could represent a compensatory attempt to open the airway before airway pressure is lowered by contraction of the DIA and the ribcage (RC) muscles.

The genioglossus (GG) pulls the tongue forward and opposes pharyngeal collapse due to inspiratory negative pressure (Remmers et al., 1978; Brouillette RT, Thach BT, 1979; Sauerland EK, Harper RM, 1976; Issa et al., 1988), as shown by earlier peaking of GG EMG activity ahead of DIA EMG activity during inspiration

(Brouillette RT, Thach BT, 1980). Phasic inspiratory GG activity decreases with sleep in normal subjects (Martin et al., 1980; Strohl KP, 1981; Onal et al., 1982), and almost ceases during REM sleep (Sauerland EK, Harper RM, 1976; Parisi et al., 1987); It, however increases significantly from wakefulness to NREM sleep, between apnoeas in OSAHS patients, and in older obese control subjects (Suratt et al., 1988). Thus, normal subjects have less activity than patients with OSAHS yet do not have occlusive apnoeas, and such augmented activation of GG in OSAHS subjects may be viewed as a protective mechanism that occurs when patency of the pharyngeal airway is compromised. Any factor that interferes with this increase in GG activity, such as onset of phasic REM sleep or periodicity of central drive, can predispose to upper airway collapse. Indeed, GG EMG activity is reduced or abolished at apnoea onset, and increased at the termination of the obstruction (Remmers et al., 1978; Suratt et al., 1988).

Muscles that cause forward movement of the hyoid bone [geniohyoid (GH), sternohyoid (SH), thyrohyoid (TH)], are thought to enlarge and stabilise the pharyngeal airway (Weigand et al., 1990; Van de Graaf et al., 1984; Van Lunteren et al., 1987; Weigand et al., 1990; Roberts et al., 1984). In both normal subjects and those with OSAHS, adoption of a supine posture is associated with forward movement of the hyoid bone (Yildirim et al., 1991). These muscles show phasic inspiratory activity, and greater mechanical activity with significant hypercapnia (Van de Graaf et al., 1984; Van Lunteren et al., 1987). Both the GH and TH show augmented and prolonged activity after occlusion at end-expiration (Van de Graaf et al., 1984). Phasic inspiratory activity of the GH is seen in normal awake subjects, with a sleep - related fall in tonic activity in all stages of sleep, and there is a negative correlation with upper airway resistance (Weigand et al., 1990).

Pharyngeal volume in anaesthetised cats displays an inverse relationship with hyoid muscle (GH, SH) length (Van Lunteren et al., 1987). Factors that influence hyoid position, such as neck flexion or mandibular abnormalities, can adversely affect the function of these muscles leading to narrowing of the hypopharynx.

Reduced activity of the tensor palatini (TP) muscle, which retracts the palate from the posterior pharyngeal wall, thereby maintaining pharyngeal patency during nasal breathing, may also play an important role in the pathogenesis of OSAHS (Sauerland et al., 1981; Tangel et al., 1991; Anch et al., 1981; Hariston LE, Sauerland EK, 1981). Tonic activity of the TP decreases during sleep and correlates with increased upper airway resistance during sleep (Tangel et al., 1991 and 1992).

The overall conclusion that can be drawn from the above studies is that a variety of different muscle groups play an important role in the maintenance of upper airway patency. Muscles that control the tongue, palate and hyoid all appear to be involved in this process, but the literature so far gives differing views on the relative importance of these muscle groups. Furthermore, it has been argued that airway compliance, independent of upper airway dilator muscle activity, may be the principal determinant of upper airway collapsibility (Strohl KP and Olson LG, 1987). The ability of the upper airway to resist collapse may, therefore, be dependant upon the relative juxtaposition of the mandible and hyoid bones, which allow for a specific pharyngeal size, and on the properties of the airway wall in the collapsible segment of the upper airway, rather than on upper airway dilator muscle activity (Strohl KP and Olson LG, 1987).

2.4.1.4.2 Impaired relationship of upper airway muscle and diaphragm contraction.

The EMG activities of upper airway muscles and diaphragm respond in a qualitatively similar manner to hypercapnia (Patrick et al., 1982), hypoxia (Onal et al., 1981), and airway occlusion (Weiner et al., 1982). This suggests that central control mechanisms of upper airway and respiratory pump muscles in humans are intimately related.

Inspiratory activation of upper airway muscles occurs earlier than activation of the DIA (Block et al., 1984), which stabilises and counterbalances the collapsing force on the upper airway by DIA and RC muscle activity (Block et al., 1984). Any reduction or delay in upper airway inspiratory muscle contraction, relative to DIA and RC muscle activity, predisposes to upper airway narrowing or collapse during sleep.

Activity of the hypoglossal nerve at lower levels of chemical drive (hypoxia and hypercapnia) is less than, and at higher levels of chemical drive greater than, phrenic nerve activity in anaesthetised dogs (Weiner et al., 1982), although allowance must be made for the fact that anaesthesia selectively inhibits neural input to the upper airway (Hwang et al., 1983). Oxygen breathing in rabbits decreases GG more than DIA EMG, whilst hypercapnia and prolonged occlusions preferentially activate GG compared to DIA (Brouillette RT, Thash BT, 1980). Non-specific respiratory stimuli (light, sound, touch) preferentially increase phasic inspiratory GG activity (Brouillette RT, Thash BT, 1980), similar to that seen with electroencephalographic (EEG) arousals at the termination of obstructive apnoeas (Remmers et al., 1978). Peripheral chemoreceptors appear to affect phasic inspiratory activity in the GG and DIA in qualitatively similar, but quantitatively different, ways. Nitrogen breathing and cyanide injection increase

phasic inspiratory activity in the GG more than in the DIA (Brouillette RT, Thash BT, 1980), and these responses are abolished by carotid body denervation.

Some reports have suggested that respiratory motor drive to the pharyngeal musculature decreases during sleep, whereas output to the diaphragm is unchanged (Remmers et al., 1980, Orem et al., 1977). Others have suggested that a preferential decrease in upper airway muscle activity is not necessary for the development of occlusive apnoeas (Onal E, Lopata M, 1982, Onal et al., 1985).

It has been hypothesised that patients with OSAHS have instability of ventilatory control similar to periodic breathing, and that occlusive sleep apnoeas occur when DIA and GG inspiratory EMG activity are both near the nadir of the cycle, which is lower than awake or sleep onset values (Onal et al., 1982). After apnoea onset, these EMG activities tend to decrease further for the first 1-3 inspiratory efforts, and then progressively increase until resolution of the apnoea, at which time GG EMG appears to increase to a greater degree than DIA EMG and for 1-2 postapnoeic breaths. The period immediately following resolution of the apnoea is usually characterised by hyperventilation of several breaths, which normalises arterial oxygen saturation (S_a , O_2). Both EMGs then decrease in activity, which predisposes to further occlusive apnoeas (Onal et al., 1982).

In addition, it has been speculated that the relative timing of inspiratory EMG activity of the upper airway to DIA and RC activity fluctuates during sleep in OSAHS (Hudgel DW, Harasick T, 1990). As an obstructive sleep apnoea approaches and upper airway inspiratory resistance progressively increases, inspiratory EMG activity of the upper airway muscles moves closer to and then falls behind RC EMG inspiratory activity (Hudgel DW, Harasick T, 1990). Activity of the upper airway muscles remains behind the RC muscles during the

apnoea, but precedes activity of the RC muscles when the upper airway opens. This could represent periodicity of the respiratory controller (Longobardo et al., 1982), with reduced damping and increased gain. During tests of upper airway collapsibility in sleeping subjects with OSAHS, there was no evidence of increased drive to upper airway dilator muscles during progressive asphyxia, despite an apparent increase in drive to the DIA (Issa FG and Sullivan CE, 1984). A clinical model of a disturbed timing relationship between upper airway and diaphragmatic contraction predisposing to OSAHS is seen in patients with diaphragmatic palsy treated with an electrophrenic pacemaker. About 50% of such patients develop OSAHS after insertion of this pacemaker (Glenn et al., 1978; Hyland et al., 1981), since the pacemaker results in DIA contraction at times other than when upper airway muscles contract. The relationship between GG and DIA is discussed further in “periodicity of central drive”.

2.4.1.5 Upper airway reflexes

Several reports indicate a role for upper airway reflex mechanism in the maintenance of patency (Horner et al., 1991). Evidence suggests that these reflex mechanism are pressure sensitive (Mathew et al., 1982 & 1984), and interference with them could lead to an imbalance between intra-pharyngeal pressure and the contraction of upper airway dilating muscles, resulting in obstructive apnoeas (Remmers et al., 1978). The importance of such protective reflexes is supported by the finding of fatal pharyngeal airway closure in rabbits, in which upper airway reflexes are abolished by topical anaesthesia (Abu-Osba et al., 1981).

Topical oropharyngeal anaesthesia (TOPA) in normal human subjects results in increased frequency of obstructive apnoeas (McNicholas et al., 1987) and

pharyngeal resistance during sleep, independent of any direct effect of lignocaine on the upper airway muscle themselves (De Weese EL and Sullivan TY, 1988). A significant increase in obstructive events was seen after TOPA in a group of otherwise asymptomatic snorers (Chadwick et al., 1991), with several subjects developing AHIs that fall within the range of OSAHS as conventionally defined (Guilleminault et al., 1976). In contrast, TOPA did not produce any significant increase in AHI or apnoea duration among patients with OSAHS, which supports the possibility that upper airway reflexes are defective in OSAHS (Deegan et al., 1993).

Defective upper airway reflexes may be a primary abnormality in OSAHS, contributing to the development of upper airway occlusion during sleep. However, such a defect could also be a secondary phenomenon, since the mechanical vibration of the upper airway, associated with loud snoring, might also blunt the afferent receptors for the reflex, which are presumed to lie in the oropharyngeal wall. Data from the above studies (Chadwick et al., 1991; Deegan et al., 1993) favour a primary abnormality in upper airway reflexes among OSAHS patients, since subjects with loud snoring would also be expected to have a mechanical vibration in the upper airway similar to that among patients with OSAHS.

Temperature sensitivity in the oropharynx in OSAHS patients is significantly impaired compared to age-matched nonsnoring control subjects (Larsson et al., 1992), which further supports the notion that upper airway reflexes are impaired in patients with OSAHS.

2.4.1.5.1 Responses to negative pressure.

Upper airway muscle EMG activity increases when negative pressure is applied to the isolated upper airway of tracheotomised rabbits (Mathew et al., 1982), probably through reflexes involving mechanoreceptors located above the trachea, and *via* several afferent pathways. Small but consistent changes in respiratory frequency were also seen in many of the animals, suggesting some involvement of the respiratory centre in these changes (Mathew et al., 1982).

In awake human subjects, the administration of sudden negative airway pressure to the upper airway leads to a pronounced and repeatable reflex increase in genioglossus activity (Horner et al., 1991). Contribution from both supra-glottic and sub-glottic receptors appears to be involved, and topical anaesthesia blocks the response when the glottis is closed (Horner et al., 1991). This response is reduced during NREM sleep (Wheatly et al., 1993). Normal awake subjects exposed to continuous negative airway pressure (CNAP) whilst supine, are able to preserve tidal volume both by immediate and sustained increases in upper airway and diaphragm muscle activity (Aronson et al., 1989).

However, during NREM sleep no immediate muscle or timing responses are seen with CNAP, and hypopnoeas and occlusive apnoea result. Re-establishment of upper airway patency is dependent on arousal and increased muscle activity. These findings suggest that protective reflexes, which act to maintain upper airway patency in the presence of negative airway pressure during wakefulness, are compromised by sleep.

2.4.1.5.2 Responses to positive pressure.

Continuous positive airway pressure, applied through the nares (nCPAP), is an effective therapy for OSAHS (Sullivan et al., 1981), and yet reduces upper airway dilator EMG activity (Deegan et al., 1993 and 1994). The efficacy of nCPAP, despite the association with reduced upper airway dilator muscle contraction, is fully consistent with the concept that suction pressures in the upper airway during inspiration cause the collapsible upper airway to occlude. This inspiratory suction pressure is abolished by nCPAP, and the reduction in upper airway dilator EMG activity during nCPAP administration is probably a consequence of the reduced need for upper airway dilating muscle contraction in the absence of any inspiratory negative suction pressure and to a possible splinting effect of the positive pressure. End-expiratory positive airway pressure has been shown to reduce the frequency and duration of apnoeas and the degree of nocturnal oxygen desaturation, in patients with OSAHS (Mahadevia et al., 1983). However, as negative pressures are still developed in the upper airway during inspiration while on external positive airway pressure (EPAP), this improvement could not be attributed to simple splinting of the upper airway. This observation suggests an improvement in other factors that may be contributing to the development of upper airway occlusion during sleep, such as decreased FRC and / or hypoxaemia (Cherniack NS, 1981).

2.4.1.5.3 Feedback from the lungs.

Pharyngeal cross sectional area (CSA) is abnormally small in obese patients with OSAHS, and varies considerably with changes in lung volume (Rubenstein et al., 1989). The mean CSA of the upper airway in snorers with OSAHS appears to be

significantly less than in non-apnoeic snorers at residual volume, but not at FRC (Brown et al., 1985).

Upper airway resistance tends to decrease with increasing lung inflation and with increasing breathing rates at low volumes (Brown et al., 1985). The above observations support the notion the vagally mediated reflexes related to lung volume can have an important influence on upper airway calibre (Van Lunteren et al., 1984).

2.4.1.6 Central factors

Abnormalities of respiratory control have been implicated in the pathogenesis of OSAHS (Onal et al., 1982), and could conceivably occur at several levels ranging from the respiratory centre to peripheral upper airway reflex mechanism.

2.4.1.6.1 Chemical drive.

The sleeping state is associated with a reduction in minute ventilation (Douglas et al., 1982), and in the ventilatory responses to hypoxia and hypercapnia (Berthon-Jones et al., 1982 and 1984), compared with wakefulness. The mechanism underlying these reductions is not thought to be due exclusively to decreased central respiratory drive (White et al., 1986), and may relate, at least in part, to mechanical changes, such as reduced upper airway patency during sleep (Skatrud et al., 1985; Hudgel et al., 1984). Support for this possibility comes from the observation that mouth occlusion pressure, which is a better index of respiratory drive than the ventilatory response (Whitelaw et al., 1975), increases from wakefulness to NREM and REM sleep in men, with little change in women; and

the mouth occlusion pressure response to hypercapnia is generally maintained during NREM sleep in comparison to wakefulness (White et al., 1986).

Upper airway resistance in OSAHS appears to be influenced by the intensity of the central respiratory drive (Series et al., 1989). At specific levels of respiratory drive post-hyperventilation, a similar decrease in central respiratory drive leads to a greater increase in pharyngeal resistance among OSAHS patients than among normal subjects, which is not explained by differences in weight and age (Series et al., 1989).

Eucapnic OSAHS patients have been reported as having a normal (Kryger et al., 1974), or reduced (Gold et al., 1993), awake hypercapnic ventilatory response, whilst obese OSAHS patients with daytime hypercapnia have reduced awake ventilatory responses to hypercapnia (Garay et al., 1981). Most patients with OSAHS are eucapnic and demonstrate augmented ventilation after apnoeas, with tidal volume of breaths as much as double that of breaths preceding apnoeas; whilst hypercapnic patients do not display this “big breath phenomenon” (Garay et al., 1981). In another study, hypercapnic ventilatory responses in obese patients with OSAHS, and in patients with obesity-hyperventilation, were significantly lower than in normal non-obese subjects subjected to abdominal mass loading, and in subjects without OSAHS (Lopata M, Onal E, 1982). However, mean DIA EMG responses in this study shows that obesity may be associated with impaired respiratory neuromuscular coupling, which in turn may impair transfer of ventilatory drive to muscle contraction (Lopata M, Onal E, 1982). Thus ventilation may be an inadequate parameter to assess central respiratory drive in these patients, and a significance ($P=0.1$) responses are likely to give a better indication of central respiratory drive in obese subjects.

It is uncertain whether the observed reduction in chemical drive is a primary defect (El Bayadi et al., 1990), or secondary to sleep apnoea, as suggested by some improvement in the ventilatory response to CO₂ in hypercapnic OSAHS patients after long-term nCPAP therapy (Berthon-Jones et al., 1987).

2.4.1.6.2 Periodicity of central drive.

Variability in inspiratory muscle timing among patients with OSAHS could result from periodicity of the central respiratory controller (Hudgel et al., 1990). During the hypopnoeic portion of the periodic breathing cycle, when ventilatory drive is low, both the relative amplitude and the relative timing of the inspiratory activity of the upper airway and chest wall muscles favour upper airway occlusion, since there is a greater fall in amplitude of upper airway muscle EMG than diaphragmatic EMG, and the normal pre-activation of upper airway EMG is not apparent (Deegan et al., 1995). On the other hand, an obstructive apnoea is terminated when the drive to the upper airway muscles is stimulated to a degree such that the magnitude of increase in upper airway dilator muscle activity exceeds that of the respiratory muscles, allowing opening of the upper airway and resumption of airflow (Deegan et al., 1995).

In addition, total pulmonary resistance can double in the period from immediately after an upper airway occlusion to immediately before the next one (Martin et al., 1980).

An arterial carbon dioxide tension (P_a , CO₂) threshold well above the eupnoeic level is observed for GG muscle stimulation during all stages of sleep and wakefulness, whilst the DIA shows increased activity at even minor degrees of hypercapnia (Parisi et al., 1987).

The maintenance of rhythmic breathing in hypoxia is dependent upon the neuro-physiological state of the higher central nervous system (CNS) (Berssenbrugge et al., 1983). Hypoxia causes periodic breathing during all stages of NREM sleep, and apnoea is produced when end-tidal CO₂ is reduced by 1-3mmHg below spontaneously breathing awake levels, with apnoea length positively correlated with the magnitude of hypocapnia. These findings point to a highly sensitive CO₂ - dependent apnoeic threshold during NREM sleep. It has been proposed that the combination of augmented peripheral chemoreceptors “gain” in hypoxia, together with the hypocapnia-induced apnoeic threshold in NREM sleep, provides the basis for the initial occurrence of apnoea, in addition to the hyperventilation that immediately follows the termination of apnoea. This hyperventilation subsequently leads to hypocapnia, which predisposes to further apnoea and contributes to the self-sustaining nature of periodic- breathing (Berssenbrugge et al., 1983).

2.4.1.6.3 Response to breath loading.

Resistive load detection thresholds during wakefulness are significantly greater among patients with OSAHS than control subjects, and the degree of load detection impairment correlates with the severity of OSAHS (McNicholas et al., 1984). A significant negative correlation between the awake ventilatory response to hypercapnia and load detection threshold was seen in both patients and control subjects. Furthermore, since awake inspiratory load compensation in patients with OSAHS is normalised after a period of nCPAP treatment, such impairment may be a reversible consequence, rather than a cause, of OSAHS (Greenberg HE, Scharf S, 1993).

If conscious factors are important in ventilatory load compensation, then the loss of these influences with sleep onset may result in an inadequate response. Normal subjects can fully compensate for external sensitive loads (Iber et al., 1982; Santiago et al., 1981; Wiegand et al., 1988) and external elastic loads (Wilson et al., 1984) during wakefulness by immediate adjustments in ventilatory timing, and minute ventilation is maintained at preloading levels. During NREM sleep, however, there is an immediate fall in minute ventilation following load application, largely due to a reduction in tidal volume. This fall becomes less marked with time due to a rise in (P_a , CO_2) that results in augmented ventilatory effort (Wilson et al., 1984).

However, it has been speculated that this lack of augmentation of respiratory drive, when a partial airway occlusion occurs during sleep, may permit forward motion of the tongue rather than the tongue being sucked backwards into the pharynx by the higher suction pressures generated with greater respiratory effort. This balance of forces could prevent the progression from partial to complete upper airway obstruction (Santiago et al., 1981).

Another factor in ventilatory load compensation is thought to be a reflex originating in respiratory muscles that are fatiguing and / or developing high intra-thoracic pressure. Neural information from these respiratory muscles is fed back to the respiratory centre, which in turn may modulate output so that the respiratory muscles are unloaded. A fatiguing respiratory pattern may occur during an obstructive apnoea (Guilleminault C, 1980), with each occluded inspiratory effort associated with increasing tension time index of the diaphragm. When this index reaches or exceeds the fatigue threshold, arousal may result, followed by opening of the upper airway (Vincken et al., 1987; Kimoff et al.,

1994). Thus, the airways may be triggered to open by a protective reflex originating in the larynx, or the inspiratory muscles, upon reaching a certain degree of contraction.

If perception of upper airway occlusion during sleep, by mechanoreceptors or inspiratory muscles, is involved in eliciting the arousal response that terminates each apnoeic event, it could be argued that elevation of the threshold for load detection might contribute to prolongation of sleep apnoeas and result in a more severe degree of asphyxia. However, the lack of prolongation of apnoea with topical anaesthesia among normal subjects (McNicholas et al., 1987), loud snorers (Chadwick et al., 1991). Patients with OSAHS (Deegan et al., 1993) could argue against the possibility of increased duration of apnoeas due to reduced upper airway pressure detection, although another preliminary report has indicated prolongation of apnoeic episode with such anaesthesia in OSAHS patients (Berry et al., 1993).

Ventilatory breathholding.

There are a number of chemical and mechanical factors that affect the duration of voluntary breathholding, a manoeuvre that stimulates some features of an obstructive apnoea (Godfrey et al., 1968). These include hypoxaemia and hypercapnia, both of which shorten maximum breathhold time. Hyperventilation lengthens the breathholding time by lowering the initial (P_a , CO_2). In addition, if a few breaths of a gas that does not alter (P_a , CO_2) are taken at the breaking point of a threshold, the subject will be able to resume the breathhold. Thus, the unpleasant sensation experienced as the breaking point is reached is not due solely to hypercapnia (Godfrey et al., 1968).

In another study, involuntary respiratory muscle contractions (recorded as waves of negative pressure) were found in most individuals during breathholding, and increased in amplitude and frequency throughout the breathholding time (Whitelaw et al., 1981). The slopes of the pressure waves (dP / dt) during breathholding were found to be greater than those in the same subjects at the same CO_2 level during rebreathing. This suggested that the response is due, in part, to a number of other, possible non-chemical stimuli (Whitelaw et al., 1981).

Effect of oxygen supplementation.

The role of O_2 desaturation in the pathophysiology of OSAHS may be assessed indirectly by observing the effects of O_2 supplementation. Nocturnal oxygen improves (S_a, O_2) in patients who have sleep-disordered breathing (Phillips et al., 1990), but there is no objective evidence of any improvement in daytime sleepiness (Gold et al., 1986), although some patients report greater alertness.

Administration of 100% O_2 acutely (Martin et al., 1982), and O_2 at $4L. min^{-1}$ throughout the night (Alford et al., 1986), eliminates (Martin et al., 1982) or reduces (Alford et al., 1986) bradycardia associated with sleep apnoea. Added oxygen increases the length of apnoeas and hypopnoeas (Gold et al., 1986), as well as increasing (P_a, CO_2), and this results in a lower pH at the end of apnoeic events (Gold et al., 1986; Alford et al., 1986). Supplemental oxygen can reduce apnoea frequency, possibly by reducing postapnoeic hyperventilation and stabilizing ventilatory drive (Gold et al., 1986).

2.4.1.7 Arousal

2.4.1.7.1 Impaired arousal responses.

Arousal from sleep in normal males is accompanied by an immediate fall in upper airway resistance to wake values (Wiegand et al., 1989), whilst termination of an obstructive apnoea is believed to depend heavily on arousal (Issa et al., 1984). Thus, arousal mechanisms may have an important role to play in the pathophysiology of OSAHS (Phillipson EA, Sullivan CE, 1978).

In normal individuals, when relief of upper airway occlusion is accompanied by arousal, there is a fall in pharyngeal resistance and a drop in end-tidal carbon dioxide tension (P_{ET} , CO_2) due to hyperventilation (Nolan et al., 1993). However, when no arousal occurs, hyperventilation is obtunded and both (P_{ET} , CO_2) and pharyngeal resistance rise.

In patients with OSAHS, evidence of arousal usually precedes or coincides with the preferential increase in upper airway tone that restores airway patency and terminates the obstructive apnoea (Remmers et al., 1978). However, the mechanisms by which airway occlusion, hypoxia, and hypercapnia lead to arousal from sleep remain unclear and it is unlikely that any single factor is responsible for arousal.

It has been hypothesised that airway occlusion activates pressure-sensitive upper airway mechanoreceptors and that these play an important role in arousal from upper airway occlusion, as nasal occlusion leads to shorter times to arousal compared to tracheal occlusions in sleeping dogs (Issa et al., 1987). The finding that topical upper airway anaesthesia significantly prolongs the time to EEG arousal in response to induced airway occlusion in normal human subjects

(Basner et al., 1992) also supports an important role for upper airway receptors in facilitating the arousal response. Responses to irritant receptor stimulation are blunted during sleep compared to wakefulness, with the degree of laryngeal and tracheo-bronchial stimulation required to produce arousal during REM sleep higher than in slow wave sleep (SWS) (Sullivan et al., 1979 and 1978). Cough and smooth muscle contraction in response to broncho-pulmonary irritant stimuli appear to be dependent on arousal, and arousal responses to such stimuli are depressed in REM sleep (Sullivan et al., 1979). Pulmonary stretch receptors stimulated by lung inflation do not cause arousal, but readily produce apnoea and tracheal smooth muscle relaxation during SWS (Sullivan et al., 1979).

Total airway occlusion during NREM sleep in normal subjects is characterized by a breath-by-breath progressive increase in suction pressure prior to arousal that is achieved by an increase in the rate of inspiratory pressure generation (Issa et al., 1983). In contrast, during REM sleep, arousal occurs after a shorter duration of airway occlusion than NREM, and the period of occlusion is associated with a rapid shallow breathing pattern. These findings are surprising, and contrast with the clinical situation in OSAHS, where apnoeas during REM sleep tend to be longer than during NREM sleep. The increasing ventilatory effort associated with the obstructive apnoea may also be an important factor that contributes to arousal, mediated by mechanoreceptors feedback from the respiratory system, probably from respiratory muscles (Kimoff et al., 1994; Gleeson et al., 1990).

Hypoxaemia stimulates specific receptors in the carotid body (Bowes et al., 1981). However, hypoxia has been shown to be poorly related to arousal in normal humans (Douglas et al., 1982), and in patients with chronic obstructive pulmonary disease (Fleetham et al., 1982). In addition, increased upper airway

resistance during sleep, below the threshold for frank apnoeas or hypopnoeas, can still produce frequent brief arousals and significant daytime sleepiness in the absence of O₂ desaturation (Guilleminault et al., 1993).

Hypercapnia, which activates receptors in the upper airway and medulla, appears to be a much more potent stimulus to arousal than hypoxia (Douglas et al., 1982).

In normal subjects, exposed to hypoxia, hypercapnia and inspiratory resistive loading during sleep, arousal occurred at different levels of blood chemistry (*Sa*, O₂ and CO₂) but the ventilatory effort for each subject was similar at the point of arousal regardless of the stimulus (Gleeson et al., 1990). It has, therefore, been concluded that increasing ventilatory effort may be the stimulus to arousal from sleep independent of the source of this rising drive to breathe (Gleeson et al., 1990).

At present, any definition of arousal from sleep will be arbitrary, since there is no universal agreement as to what exactly constitutes an arousal. This difficulty in defining arousal relates largely to the limitations of the standard Rechtschaffen and Kales (Rechtschaffen A and Kales A, 1968) criteria, which remain the current gold standard for staging sleep. Newer criteria, based on spectral analysis of the EEG during sleep (Salinsky et al., 1988), will almost certainly improve the ability to classify arousal, and the advent of computerised software for EEG analysis will facilitate this development. A preliminary report, based on spectral analysis of the EEG, has demonstrated that the arousal associated with the termination of obstructive apnoea is not a sudden event that occurs at the termination of apnoea, and that there is evidence of partial arousal developing from much earlier on during the course of the apnoeic episode (Rees et al., 1993).

The arousal response does not usually lead to complete awaking, but rather may cause lightening of sleep, with a shift from a deeper sleep stage to higher stage. Alternatively, there may be no formal change in sleep stage by conventional definition, but short bursts of alpha waves may occur at the termination of apnoea. These sleep stage / state changes lead to sleep fragmentation, which in turn can worsen the underlying OSAHS (Guilleminault C, Rosekind M, 1981).

2.4.1.7.2 Postapnoeic hyperventilation.

All apnoeic events do not necessarily end with an EEG arousal, whilst EEG changes are not essential for an arousal response to have occurred. Nevertheless, the above data support the view that arousal represents a protective mechanism to restore ventilation, and normalise blood gasses, whenever the upper airway is occluded. Thus, any factor that interferes with the arousal mechanism could lead to more profound and prolonged apnoeas. However, arousal alone could potentially predispose to further apnoeas by virtue of the hyperventilation that occurs with relief of upper airway occlusion (Nolan et al., 1993). The resultant fall in (P_{ET} , CO_2) and (Sa , O_2) will predispose to further occlusion of a compromised upper airway.

Integrated Pathophysiology of OSAHS

The foregoing discussion indicates the complexity of the pathophysiology of OSAHS. Various factors, ranging from upper airway anatomy to central respiratory control mechanisms, interact to produce the clinical syndrome of OSAHS. Different factors will predominate in individual patients, but it is likely that all patients with clinically significant OSAHS have a multifactorial aetiology,

rather than any single causative factor. Specific anatomical narrowing of the upper airway occurs in only a subgroup of patients with OSAHS (Guilleminault et al., 1976), and thus other factors are likely to play a role in the development of the clinical OSAHS syndrome. However, these factors, such as defects in ventilatory control and protective upper airway reflexes, are less easily defined and further research is needed to elucidate their precise role in maintaining upper airway patency during sleep.

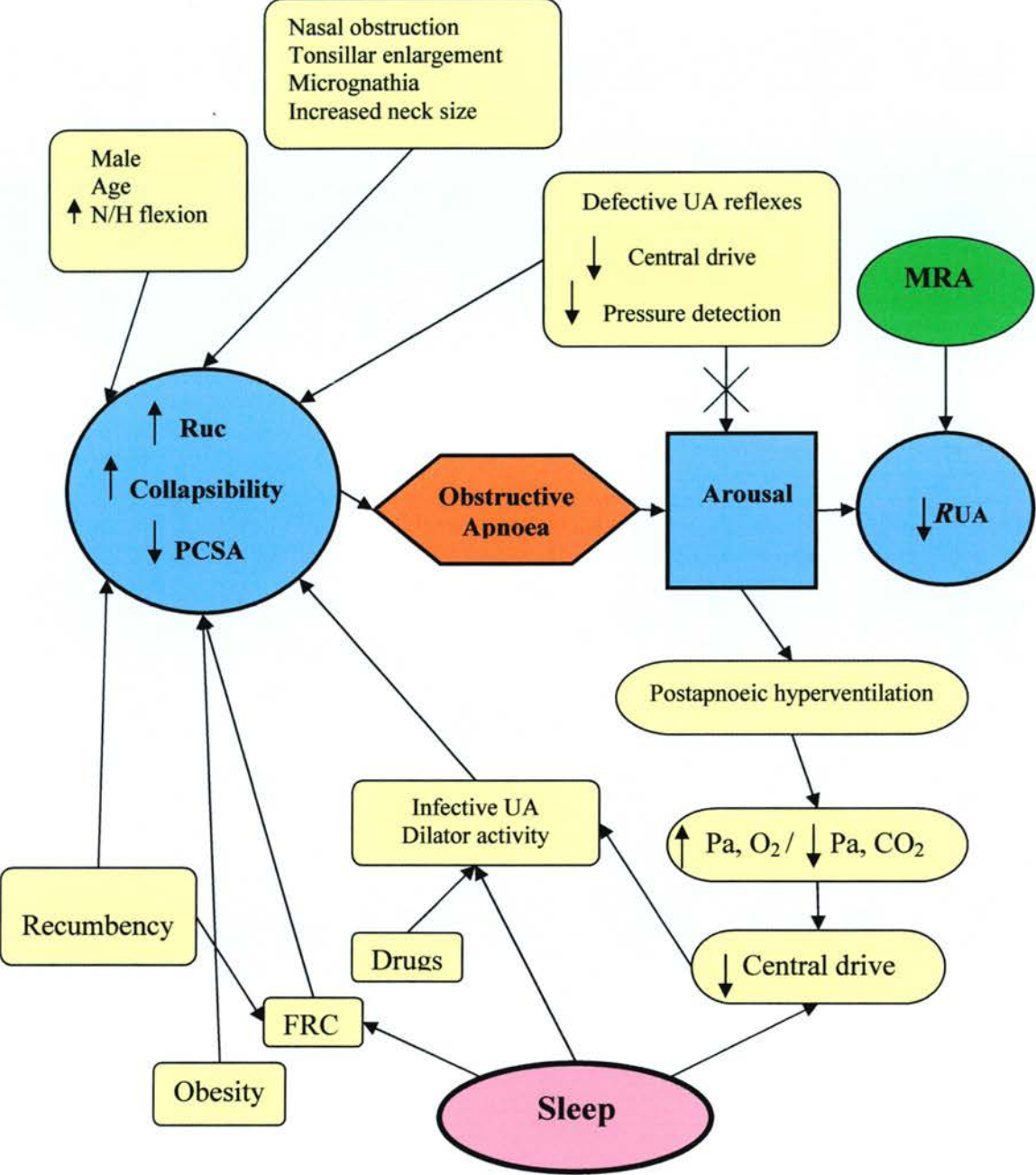
The role of central factors in the development of OSAHS is underlined by reports in the early literature related to OSAHS that successful relief of OSAHS by tracheostomy is frequently followed by evidence of central sleep apnoea (Guilleminault C, Cumiskey J, 1982). Furthermore, the division between central and obstructive sleep apnoea / hypopnoea syndrome is not as clear cut as it might appear, since many patients with central sleep apnoea present with clinical features more suggestive of OSAHS (Bradley et al., 1986), and it is possible that in some patients, upper airway occlusion reflexly triggers a central, rather than an obstructive apnoea. Support for this notion comes from the finding that some patients with central sleep apnoea can be successfully treated with nCPAP (Bradley et al., 1986).

A better understanding of the interacting factors that lead to the development of clinically significant OSAHS will hopefully, lead to the development of better modalities of therapy.

A schematic illustration of the integrated pathophysiology of OSAHS is given in figure 2.3 (Deegan et al., 1995). This illustration underlines the complexity of the overall pathophysiology, but emphasizes the central features, with factors that

compromise upper airway patency and promote obstruction on one hand and other factors, principally arousal, which acts to restore upper airway patency.

Fig 2.3 Schematic illustration of the integrated pathophysiology of OSAHS



UA: Upper airway
 H/N: Head and neck
 RUA: Upper airway resistance
 PCSA: Pharyngeal cross sectional area
 FRC: Functional residual capacity
 Pa, O₂: Arterial oxygen tension
 Pa, CO₂: Arterial carbon dioxide tension
 X: Impairment of arousal mechanism
 MRA: Mandibular Repositioning Appliance

2.4.2 Anatomical Factors

A number of cephalometric studies have demonstrated characteristic differences in the craniofacial anatomy and oropharyngeal dimensions of people suffering from OSAHS (Lyberg et al., 1989; Lowe et al., 1986; Solow et al., 1993; Jamieson et al., 1986; Tangugsorn et al., 1995; Battagel et al., 1996; Ozbek et al., 1998; Kulnis et al., 2000).

2.4.2.1 Reduced cranial base length

It is a consistent finding of cephalometric studies of OSAHS subjects, (Bacon et al., 1988). As a logical consequence, the lengths of the maxilla and of the bony pharynx are diminished. These measurements are confirmed by Battagel et al., (1996), who suggests a mean decrease in cranial base length of some 2.4mm and identifies a consequential of the antero-posterior dimensions of the cranium with subsequent 'Retrusion of the face'.

2.4.2.2 Reduced cranial base angle

This has been detected in a significant proportion of OSAHS subjects (Jamieson et al., 1986). Battagel et al., (1996) measure this decrease (Ba-SN) as being approximately 3.7° in OSAHS subjects as compared with controls. Jamieson and his colleagues, hypothesize that the more acute cranial flexure, is associated with a lower hyoid position and abnormal development of the hypo-pharyngeal soft tissues.

2.4.2.3 Increased cranio-cervical angle

De-Berry Borowiecki et al., (1988), suggest that abnormal growth and pathological changes in the cervical column to influence the axial posture and can also affect the position of the hyoid bone and other related structures. He found that a significant number of OSAHS patients showed distinctive changes in the body of the cervical vertebra compared to a control groups. In all of these cases, the abnormality appeared as a flattening of the body of the fourth vertebrae and an extra bony ridge on its anterior border. Whilst Solow et al., (1993) detected an increased cranio-cervical angle; he related this to a probable postural response to reduced upper airway patency, rather than to a specific cervical anatomical abnormality. He cites Cote (1988), who states that ‘although no formal description of the head posture in this condition has been made; an extended head posture is generally recognised by clinicians as being a characteristic appearance of patients with OSAHS’. Although the cranio-cervical angle appears particularly sensitive to differences in recording methodology (Solow and Tallgren 1971), it has become obvious that a significant increase is associated with reduced patency of the upper airway. Indeed, Solow measured a mean increase of 12° , which he attributed to a forward inclination of the vertebral column rather than an upward rotation of the head itself. This contrasts with his earlier findings in growing patients with adenoidal hyperplasia and other upper airway patency problems, where measured increases were smaller (2° mean) and mediated by a true extension of the head. This is explained by the need for non-growing individuals to maintain the visual axis in its horizontal position. This concept of postural compensation to upper airway obstruction is very much aligned with the earlier realisation that airway

patency, or lack thereof, can lead to certain specific growth patterns of the facial skeleton.

2.4.2.4 Inferiorly positioned hyoid bone

Hyoid bone position has been reported to be significantly inferior in OSAHS subjects as compared to control groups (De-Berry Borowiecki et al., 1988; Tsuchiya et al., 1992; Johns et al., 1998; Battagel et al., 2000). In 1987, Djupesland concluded that, 'with regard to skeletal morphology, the most outstanding feature in OSAHS subjects is the more inferior position of the hyoid bone. In such patients, the hyoid is consistently located at the level of the cervical vertebra C4-C6, compared with the C3-C4 level in controls'. He suggests that as the hyoid is an anchor for the musculature comprising the tongue, a more inferior hyoid position would result in a greater mass of the tongue being located at the hypopharyngeal level and therefore the base of the tongue would be in a more upright position. The altered hyoid position has been suggested by some to be strictly vertical with no indications for its mal-alignment in the antero-posterior dimension (Kuna et al., 1988). Others have reported an infero-anterior position (Rivlin et al., 1984), which may involve some slight rotation.

Partinen (1988) suggests a link between hyoid position relative to the cervical vertebrae to the severity of OSAHS (in terms of RDI/AHI) and to Posterior Airway Space, (the measured distance from the base of the tongue to the posterior pharyngeal wall).

Young and McDonald (2002) found also the hyoid bone to be more inferiorly positioned in the OSAHS than the controls.



2.4.2.5 Bimaxillary retrusion

Bimaxillary Retrusion or retrognathia of the mandible alone has been reported (Jamieson et al., 1986; Tsuchiya et al., 1992) in up to 42% of subjects in a number of OSAHS investigations, and recent work undertaken by Battagel JM, (1996), has shown significant reductions in mandibular length Go-Me reduction of up to 5.9mm), and even variations among mandibular plane inclinations are accounted for similar results were obtained. Other studies (De-Berry Borowiecki et al., 1988) have shown no indication of this trait and we must accept that while a decrease in mandibular body length has often been described, this does not appear to be a universal finding.

2.4.2.6 Increased lower facial height

Lowe et al., (1986); Bacon et al., (1990); Tsuchiya et al., (1992) found that there is increase in the lower facial height with concomitant increase in the maxillo-mandibular planes angle.

2.4.2.7 Reduced width of oropharynx

Djupesland et al., (1987) found that up to 50% reduction in diameter at the level of the soft palate. More recently, Battagel et al., (1996) found that for all measurements, the mean airway dimensions in OSAHS subjects are approximately 66% of those found in control groups. Interestingly, these dimensions are reported to be consistently reduced, regardless of the subject being erect or supine (Yildirim et al., 1991).

2.4.2.8 Increased soft palate dimensions

The soft palate has been found to be longer (Jamieson et al., 1986; Bacon et al., 1988; Partinen et al., 1988; Lyberg et al., 1989; Riley et al., 1988), larger and in contact with a wider area of the tongue (Lyberg et al., 1989). Interestingly, comparison of two sleep disordered groups, (OSAHS and simple snorers without OSAHS) reveal very few significant differences in cephalometric measurements, however, the soft palate in OSAHS subjects is found to be larger and thicker as compared to those in patients who snore in isolation (Battagel et al., 2000).

2.4.2.9 Increased tongue size

Data regarding the tongue is ambiguous. Whilst Lyberg (1989) found no difference in tongue size in OSAHS subjects, De-Berry-Borowiecki et al., (1988) and Lowe et al., (1986 and 1991) found it to be significantly larger as compared to control groups. Among others, Partinen et al., (1988) has suggested that although the tongue size may be normal, very often a reduced inter-maxillary space means that the area in which it functions is smaller. That is, in relative terms the tongue is enlarged.

Lowe et al., (1986a) found moderate to severe sufferers of OSAHS tended to have a posteriorly positioned maxilla and mandible, a steep occlusal plane, overerupted maxillary and mandibular teeth, proclined incisors, a steep mandibular plane, a large gonial angle, high upper and lower face heights and an anterior open bite in association with a long tongue and a posteriorly placed pharyngeal wall (Cistulli, 1996).

Palatal flutter has been reported to be the most important cause of snoring (Ellis et al., 1993). In situations of airway obstruction, the blockage is often located at the

level of the soft palate, but has also been identified elsewhere within the entire extent of the pharynx (Ellis et al., 1993; Croft et al., 1991; Lugaresi et al., 1989).

Colmenro et al., (1991) found OSAHS associated with maxillofacial abnormalities such as temporomandibular joint (TMJ) ankylosis with micrognathia, Treacher Collins Syndrome and Long Face Syndrome. The combination of a retropositioned facial skeleton and reduced oropharyngeal dimensions, at one or more sites between the soft palate, tongue and pharyngeal wall, partly explains the underlying aetiology of this condition.

2.5 CLINICAL SYMPTOMS

Clinically, patients exhibit a number of characteristics, which may be considered typical of OSAHS. These may be divided into nocturnal and diurnal symptoms:

2.5.1 Nocturnal Symptoms

- Snoring
- Choking
- Abnormal motor activity
- Nocturia
- Dry mouth

2.5.1.1 Snoring

The most obvious night-time problem is loud snoring, although this frequently more of a dilemma for the rest of the family than the subject himself. A characteristic pattern in OSAHS is that of loud snoring with associated snorting, interrupted by episodes of silence (apnoeic episodes) and breaks off suddenly as air finally enters the lungs (Guilleminault C et al., 1976; Kales A et al., 1985).

Whilst a high percentage of OSAHS subjects snore, the majority of people who snore do not have OSAHS (Battagel, 1996). A significant percentage of these people who snore suffer from OSAHS (Lowe et al., 1992). Woodhead et al., (1991), correlated factors with OSAHS such as excessive loud snoring, a decrease O_2 , narrow oropharynx, marked obesity, and increased neck dimension.

Snoring was once considered to be harmless; (Kleitman N, 1963) but now is suggested to be indicative of a significant clinical problem, whose medical

consequences range from no physical debilitation to failure to thrive (Loughlin GM, 1992; Marcus et al., 1994). It has been estimated that as many as 70% of adults with OSAHS snored during childhood (Guilleminault C, Dement WC, 1978). Those with OSAHS are at increased risk for hypertension, cardiovascular disease, cerebro-vascular disease, and impaired function caused by sleepiness (Guilleminault C, Dement WC, 1978; Koskenvuo et al., 1985; Hoffstein V, Mateika S, 1994; Ulfberg et al., 1996; Young et al., 1996).

Epidemiologic studies of habitual snoring in children suggest a prevalence of between 7% and 12% (Ali et al., 1993 and 1994; Owen et al., 1996; Corbo et al., 1989). Snoring children are reportedly mouth breathers (Owen et al., 1996; Carroll et al., 1995) or restless sleepers, (Ali et al., 1993 and 1994; Owen et al., 1996) have excessive daytime sleepiness, (Ali et al., 1993 and 1994) are hyperactive, (Ali et al., 1993 and 1994) have poorer hearing, (Owen et al., 1996) and present with previous adenoidectomy and enlarged tonsils (Nieminen et al., 1997). Although snoring has been reported to be a common finding in children with symptomatic OSAHS, (Nieminen et al., 1997; Westbrook PR, 1983; Brouillette et al., 1982; Gastaut et al., 1966; Lugaresi et al., 1978; Bacon et al., 1990) only a subgroup of habitually snoring children have OSAHS (Carroll et al., 1995).

Genetic and environmental factors influence snoring, and many studies support an anatomic origin (Bacon et al., 1990; Isono et al., 1996). Palatal flutter has been reported to be the most important cause of snoring (Ellis et al., 1993). In situations of airway obstruction, the blockage is often located at the level of the soft palate, but has also been identified elsewhere within the entire extent of the pharynx (Ellis et al., 1993; Croft CB, Pringle M 1991; Lugaresi et al., 1989).

2.5.1.2 Choking

A sensation of choking or dyspnea that interrupts sleep is reported by 18% to 31% of patients (Coverdale SGM et al., 1980; Kales A et al., 1985; Maislin G et al., 1995). During episodes of upper airway obstruction, progressively more vigorous inspiratory efforts lead to more negative intrathoracic pressure swings, with an increase in venous return. This may increase the pulmonary capillary wedge pressure and contribute to the sensation of dyspnea (Buda AJ et al., 1981). Nocturnal dyspnea from OSAHS usually resolves quickly on awakening, whereas the paroxysmal nocturnal dyspnea that is characteristic of congestive heart failure patients takes much longer to resolve.

2.5.1.3 Abnormal motor activity

About half of OSAHS patient report restless sleep (tossing and turning) and diaphoresis, usually in the neck and upper chest area (Coverdale SGM et al., 1980; Maislin G et al., 1995), and involuntary leg movement during sleep (Johal A, 1998). These symptoms are probably related to the increased breathing efforts during periods of upper airway obstruction.

2.5.1.4 Nocturia

Nocturia is a relatively common symptom in OSAHS (Hoffstein V and Szalai JP). Twenty eight percent (28%) of patients with OSAHS reported 4-7 nightly trips to the bathroom (Hajduk IA et al., 2003). Increased intra-abdominal pressures, confusion associated with arousals, and increased secretion of atrial natri-uretic peptide have been proposed contributors to nocturia (Krieger J et al., 1989).

2.5.1.5 Dry mouth

About 74% of patients with OSAHS reported dry mouth and the need to drink water either in the morning or during the night (Kales A et al., 1985). Drooling occurs in 36% (Kales A et al., 1985). These symptoms are most likely the result of mouth breathing, commonly seen in patients with OSAHS (Ohayon MM et al., 2001).

2.5.2 Diurnal (daytime) symptoms

The daytime symptoms are associated with the poor quality of the previous night's sleep and include:-

- Hypersomnolence (excessive daytime sleepiness)
- Depression and psychological dysfunction
- Headaches
- Sexual problems (Decreased libido)
- Impaired concentration
- Renal failure

2.5.2.1 Hypersomnolence (Excessive daytime sleepiness)

Excessive daytime sleepiness (EDS) is a frequent symptom of patients with obstructive sleep apnoea / hypopnoea syndrome (OSAHS). Poor quality of nightly sleep may have a profound effect upon the subject during their daily activity. Upon working, subjects often report feeling unrefreshed and 'not having slept well', (Johal A, 1998). Findley et al., (1988), acknowledged the frequent finding, that in extreme cases, subjects may fall asleep if not being physically or mentally

stimulated. Often the sleepiness is more obvious to others in the environment than to the subjects themselves.

Driving a car presents an additional danger and reports of falling asleep at the wheel are not uncommon (Battagel et al., 1996). In a study by Findley et al., (1988), 24 per cent of a group of OSAHS sufferers reported feeling drowsy whilst driving, at least once per week. Aldrich MS, (1989) found that 31 per cent of drivers with OSAHS had been involved in a road traffic accident within the last 5 years. Stradling et al., (1991) suggested that snoring alone causes hypersomnolence without associated sleep apnoea or hypopnoea. Long distance lorry driving and piloting aircraft are occupations, which can prove fatal (Battagel et al., 1996).

The Royal College of Physicians of England (1993) report stated that 20-25% of motorway accidents in U.K are due to drivers falling asleep at the wheel; OSAHS may have a very important role in causing accidents.

Sauter et al., (2000) claimed that excessive daytime sleepiness (EDS) is a high-risk factor for accidents at work and on the road. Thirty untreated patients with different levels of severity of OSAHS were studied concerning night sleep and EDS. The criterion for severity was the respiratory disturbance index (RDI): 15 patients were classified as 'moderately' apnoeic ($RDI < 40$), 15 as 'severely' apnoeic ($RDI > 40$). Following nighttime polysomnography, objective and subjective aspects of EDS were studied. To assess objective EDS the Maintenance of Wakefulness Test (MWT) and a computer-based vigilance performance test were used. Subjective EDS was determined using the Stanford Sleepiness Scale (SSS), the Epworth Sleepiness Scale (ESS) and the Visual Analogue Scales for Performance (VAS-P) and Tiredness (VAS-T). Well-being was assessed using the

Scale of Well-Being by von Zerssen (Bf-S/Bf-S'). Severe apnoea patients spent more time in stage 1 and less in slow-wave sleep. MWT latencies tended to be shorter in the severe apnoea group. Vigilance testing revealed no group differences. Patients with moderate apnoea described themselves as more impaired in all subjective scales, but only SSS scores reached statistical significance. Their results suggest that there is no simple correlation between polysomnographic and respiratory sleep variables at night on the one hand, and the extent of EDS on the other hand. Furthermore, subjective and objective evaluation of EDS does not yield the same results.

2.5.2.2 Depression and psychological dysfunction

Sleep changes, most notably disturbances of REM sleep, is intrinsic to depression; OSAHS causes predominantly REM sleep disturbances, (Kaplan R, 1990). Relief of mild to moderate sleep and breathing disorders in children is associated with improved behaviour and psychological functioning (Ali et al., 1996).

Personality changes and abnormal behaviour have both been reported as a consequence of nocturnal sleep fragmentation and subsequent EDS. Aggressive and irritable behaviour is typical, with elevated level of anxiety, paranoia and depression is also reported (Wright et al., 1997). Hypnagogic hallucinations have also been reported as a possible consequence of a severe OSAHS condition (Wright et al., 1997).

2.5.2.3 Headaches

Morning headaches is reported in about half of the OSAHS patients and often are described as dull and generalized (Kales A et al., 1985). They usually last 1-2

hours and may prompt the ingestion of analgesics. A study from the headache clinic found OSAHS to be the main cause of nocturnal or morning headache (Paiva et al., 1997).

2.5.2.4 Sexual problems

Abatement of sexual drive or impotence has been reported in patients with OSAHS (Karacan et al., 1995). One third of the patients report decreased libido or impotence, which tends to improve with treatment (Kryger et al., 2005).

2.5.2.5 Impaired concentration

Many reported inability to concentrate, poor memory and temporal disorientation (Johal A, 1998), which further complicate the situation, leading to an inability to remember everyday items such as appointments and telephone numbers (Battagel JM, 1996). Personality changes, such as aggressiveness, irritability, anxiety, or depression may also be observed (Kryger et al., 2005).

2.5.2.6 Renal failure

Hui et al., (2000) studied patients with end-stage renal failure (ESRF) who are reported to have a high prevalence of sleep disorders, such as daytime sleepiness, insomnia, restless legs syndrome (RLS), and obstructive sleep apnoea / hypopnoea syndrome (OSAHS). However, there is published data from Southeast Asia. A sleep questionnaire was administered to 201 patients (103 men) at continuous ambulatory peritoneal dialysis (CAPD) outpatient clinic to assess sleep problems. Patients had a mean age of 56.7 ± 12 (SD) years, with a mean body mass index (BMI) of 23.6 ± 3.5 kg/m². Daytime sleepiness was the most

frequent symptom (77.1%), and frequent awakening occurred in 69% of the patients. Sleep-onset insomnia and sleep-maintenance insomnia occurred in 73% and 60% of the patients, respectively. Sixty-two percent of the patients reported symptoms of RLS, which significantly correlated with sleep-onset insomnia (*odds ratio [OR], 2.9; 95% confidence interval [CI], 1.5 to 5.5; P = 0.001*) and sleep-maintenance insomnia (*OR, 2.1; 95% CI, 1.2 to 3.8; P = 0.014*). The prevalence of OSAHS was estimated by the frequency of the following symptoms: extremely loud snoring, 7 patients (3.5%); observed choking, 21 patients (10.5%); witnessed apnoea, 11 patients (5.6%); snoring and witnessed apnoea, 6 patients (3%); disruptive snoring, 29 patients (14.4%); and disruptive snoring and witnessed apnoea, 3 patients (1.5%). This questionnaire survey confirmed a high prevalence of daytime sleepiness, insomnia, and RLS in patients with ESRF undergoing CAPD but showed a relatively low prevalence of OSAHS of up to 14.4%, which may be related to the low BMI of these patients with ESRF compared with other populations.

The dominant symptoms of OSAHS are excessive daytime sleepiness, impaired concentration and snoring (SIGN, 2003).

2.6 MEDICAL COMPLICATIONS

- Hypertension
- Cardiac arrhythmias
- Coronary heart disease and left ventricular hypertrophy
- Stroke (Cerebro-vascular accidents)
- Psychotic disorders
- Mortality

2.6.1 Hypertension

Blood pressure and number of patients with hypertension increased linearly with severity of sleep apnoea, as shown by the apnoea/hypopnoea index. Multiple regression analysis of blood pressure levels of all patients not taking antihypertensives showed that apnoea was a significant predictor of both systolic and diastolic blood pressure after adjustment for age, body mass index, and sex. Multiple logistic regression showed that each additional apnoeic event per hour of sleep increased the odds of hypertension by about 1%, whereas each 10% decrease in nocturnal oxygen saturation increased the odds by 13% (Lavie Peretz et al., 2000).

Lavie et al., (2001) have demonstrated that hypertensive patients with sleep apnoea whose blood pressure responds beneficially to treatment have less severe sleep apnoea than those patients whose blood pressure remains elevated despite anti-hypertensive therapy. Since neither obesity nor nocturnal hypoxaemia appear to be important determinants of ineffective treatment, we suggest that resistant hypertension may be caused by frequent intermittent sympathetic stimulation.

2.6.1.1 Systemic hypertension

Short-lasting rises in blood pressure are a recognized feature associated with nocturnal apnoeas (Fletcher EC, 1995), however such rise have not, as yet, been linked with adverse prognostic outcomes. Kales et al., (1984) found a high prevalence of OSAHS in hypertensive patients. Hirshkowitz et al., (1989) found a higher level of OSAHS only in the subgroup of hypertensive patients receiving drug therapy with erectile complaints.

Hoffstein et al., (1988) found AHI positively associated with diastolic blood pressure but in contradiction, mean oxygen saturation was also positively associated. Levinson et al., (1991) concluded that the evidence of a link between obstructive sleep apnoea / hypopnoea syndrome and hypertension is conflicting and at present inconclusive.

2.6.1.2 Pulmonary hypertension and right sided heart failure

Patients with OSAHS had a high prevalence of pulmonary hypertension [$^{13}/_{22}$ (59%) and $^8/_{12}$ (67%)] (Schroeder et al., 1978; Tilkian et al., 1976). Pulmonary hypertension (PH) and daytime hypoxaemia were associated with either chronic airway obstruction or with severe obesity (Apprill et al., 1991).

Kreiger et al., (1989) and Weitzenblum et al., (1988) found a prevalence of pulmonary hypertension (pulmonary arterial pressure > 20 mmHg) in about 20% of patients studied. After regression analysis, significant correlation was found between pulmonary arterial pressure and arterial blood gas levels (P_a , O_2 and P_a , CO_2) and indices of lung function.

Bradley et al., (1985) did find a significantly lower nocturnal O_2 saturation in six patients clinically diagnosed as having right heart failure, as well as P_a , O_2 and

lung function indices. All six were smokers and the classification of heart failure is of uncertain validity.

2.6.2 Cardiac arrhythmias

Cardiac arrhythmias (Dysrhythmias) is the disturbance of the heart rhythm or gross disturbances of heart rate which are usually caused by lesions of the sinoatrial or atrioventricular nodes, or of the cardiac conducting tissues, sometimes by drugs. Most dysrhythmias reduce cardiac efficiency and cardiac output.

Shepard et al., (1985) documented arrhythmias in 74% of a group of OSAHS patients. Patients with severe apnoea may experience cardiac arrhythmias associated with oxygen desaturation below 70% (Miller WP, 1982). Extreme sinus bradycardia (heart rate less than 30), tachycardia (abnormally rapid heart rate), sinus arrest and atrio-ventricular block have been observed in patients with OSAHS. These may result in anoxic seizure, cardiac arrest and sudden death (Kryger et al., 1974).

Flemons et al., (1993a) however concluded that currently no evidence to suggest that patients with OSAHS are at increased risk of cardiac arrhythmias during sleep.

2.6.3 Coronary heart disease and left ventricular hypertrophy

Hedner et al., (1990) found that OSAHS patients had a significantly higher left ventricular mass index than controls (Approx. 15% higher), but no polysomnography was carried out to diagnose OSAHS and the influence of important confounding variables was poorly assessed. Hanly et al., (1992) found

no significant association even without consideration of confounding variables such as age, smoking and hypertension.

Schmidht-Nowara (1990) studied the association of apnoeic index and coronary heart disease in the general population but the results are of limited validity. Davies et al., (1994) concluded that there is no good evidence that patients with OSAHS have an increased risk of left ventricular hypertrophy, cardiac failure or coronary heart disease.

2.6.4 Stroke (Cerebro-vascular accidents)

Strokes are a common cause of disability and death, especially in the elderly (Scully C and Cawson RA, 2000).

Mohsenin V and Valor R, (1995) reported statistically significant difference in the AHI between 10 patients with hemispheric strokes and 10 matched controls. The major difficulty in these associations between sleep apnoea and stroke is in distinguishing which comes first as a consequences or cause.

Patients with OSAHS have been estimated to suffer cerebro-vascular accidents at three to six times the rate of controls (Friedlander et al., 1998). Atherosclerosis of the cervical portion of the carotid artery has been suggested as the possible cause of these strokes. Calcified lesions are found typically in the region of C3 and C4 (Friedlander et al., 1998). These atheromas are visible on lateral cephalograms and the prevalence has been recorded as high as 21.3% in patients with OSAHS (Friedlander et al., 1998).

2.6.5 Psychotic disorders

There is increasing recognition of the link between OSAHS and depression. Sleep changes are intrinsic to depressive disorders, most notably in REM sleep. The features of depression are similar or indicated by the symptoms of OSAHS (Kaplan R, 1990). The author suggested the implications are two fold - OSAHS needs to be excluded in cases of chronic or resistant depression and treatment of OSAHS will make it easier to treat the primary depressive disorder.

2.6.6 Mortality

One of the key issues about OSAHS and its effect on health is whether patients have an increased risk of mortality from the disease compared to the general population.

Gonzalez-Rothi et al., (1988) produced the best-designed study, including a control group, full follow-up of the study sample, validation of deaths from death certificates and use of regression analysis. There was no significant difference in mortality for patients with OSAHS whether treated or untreated.

Partinen et al., (1988) found that conservatively treated patients had a significantly greater risk of vascular mortality compared to patients treated with tracheostomy.

Bliwise et al., (1988) found no significant association between AHI and risk of mortality with age having the main association. Ancoli-Israel et al., (1989) found a significant association between mortality and AHI in women but not in men.

There is little evidence from the available studies to conclude that OSAHS is associated with an increased risk of mortality (Royal College of Physicians of England, 1993).

Fig 2.4

Natural history of OSAHS

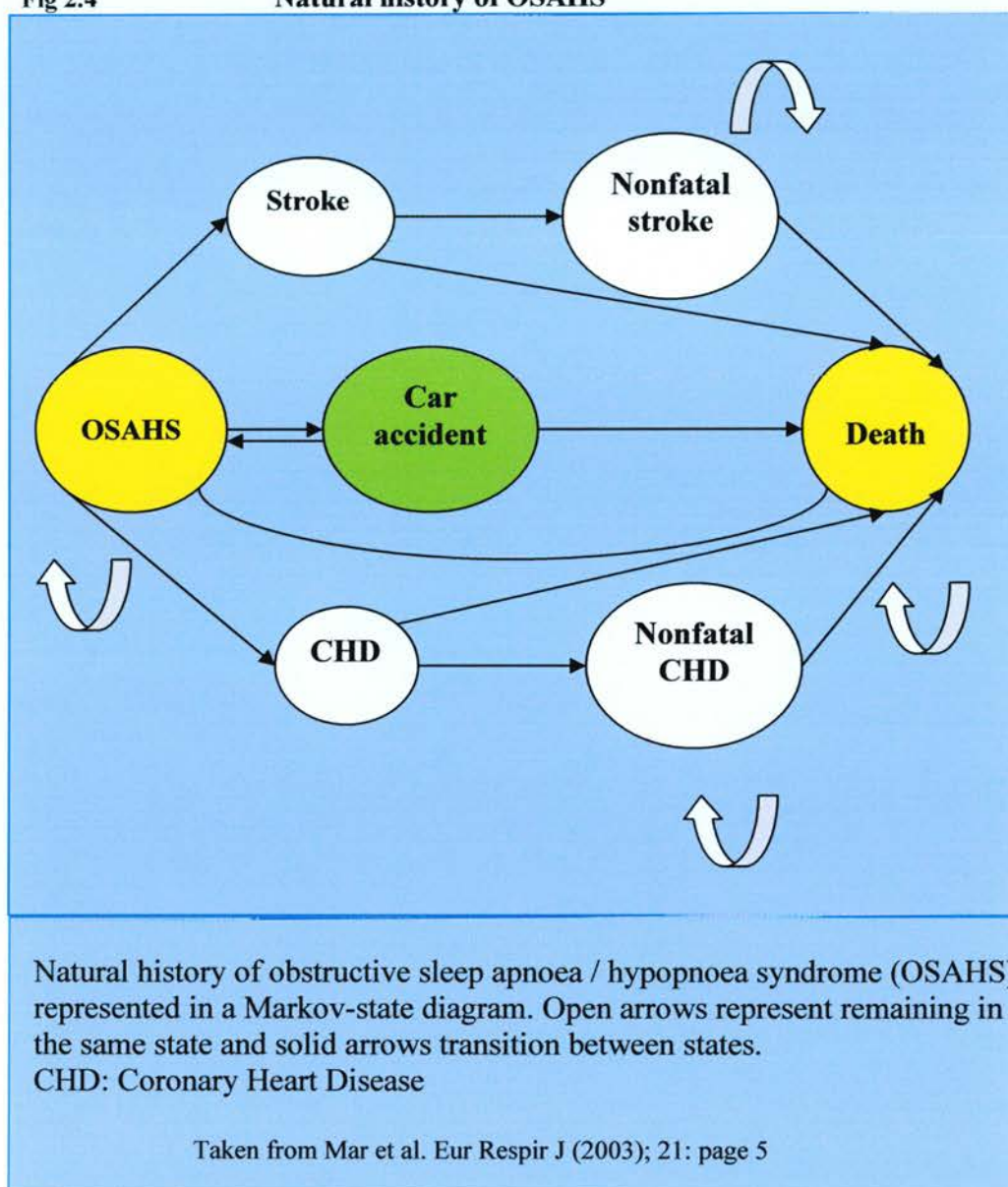


Table 2.2 Conditions associated with sleep apnoea

Oropharyngeal narrowing

Enlarged tonsils / adenoids
Lingual hypertrophy
Micrognathia
Tumour
Mandibular malformations
Nasal septal defects
Allergic nasal obstruction
Vocal cord paralysis

Endocrine disorders

Hypothyroidism
Cushing's disease
Acromegally
Panhypopituitarism
Obesity
Diabetic autonomic neuropathy

Musculo-skeletal disorders

Myasthenia gravis
Muscular dystrophy
Kyphoscoliosis

Neurological disorders

Brain stem infarct or tumour
Encephalitis
Bulbar poliomyelitis
Motor neurone disease
Head trauma
Autonomic dysfunction (Shy-Drager)

From: Nasser S, Rees PJ. Consequences of sleep apnoea. BJCP, 1992; 46:1

2.7 DIAGNOSIS

The clinical diagnosis of OSAHS depends on the identification of several symptoms and causes so that treatment can be appropriately directed to the cause.

These include:

History and Clinical Examination

Investigations:

- ◆ Cephalometric radiography
 - *Measurements of The Face and The Cranium*
 - *Soft Tissues Measurements*
 - *The Cervical Spine and Hyoid Bone*
 - *Oral and pharyngeal Measurements*
- ◆ Computer tomography scanning
- ◆ Magnetic resonance imaging
- ◆ Polysomnography
- ◆ Oximetry
- ◆ Fluoroscopy
- ◆ Acoustic reflectance technique
- ◆ Fibroptic and nasal endoscopy
- ◆ Nasal capnography
- ◆ Questionnaires

2.7.1 History and Clinical Examination

In term of diagnosis, a comprehensive history and clinical examination may be suggestive of OSAHS, but for confirmation, other investigations are required. The

examination should include an ear, nose and throat assessment, so that any physical obstructions to breathing may be identified. History taking and physical examination are the simplest methods used to diagnose OSAHS. For complete history data capture, it is essential that the subject to be accompanied by his sleeping partner. Whilst the subject will be aware of how he/she feels during the day, a partner is more likely to be able to describe the degree of nocturnal disturbances.

2.7.1.1 History

The history should include the patients 'and the partners' summary of symptoms such as choking attacks, morning headaches, gastro-oesophageal reflex, nocturia, impotence, poor memory and concentration and mood changes (McNamara et al., 1993). The cardinal features of OSAHS are however snoring and daytime sleepiness (Kaplan R, 1990; McNamara et al., 1993).

Indices have been developed to aid diagnosis, the first of which is the most commonly used.

2.7.1.1.1 Epworth sleepiness scale (ESS)

This is a questionnaire which has been designed to assess how likely a person would be to doze off in the following eight situations:-

- sitting and reading;
- watching television;
- sitting inactive in a public place (eg. a theatre or meeting);
- a passenger sitting in a car for an hour;
- lying down to rest in the afternoon;

sitting and talking to someone;

sitting quietly after lunch, without having consumed alcohol;

and as the driver of a car, stopped for few minutes in traffic.

Scores run from zero (no chance) to three (high chance) with one equalling a low likelihood and two a moderate probability. The maximum possible score therefore is 24. Scores of more than 15 (that is over 50%) suggest that the subject is sleepier than would be considered normal and perhaps should seek treatment.

2.7.1.1.2 Apnoea / hypopnoea index (AHI)

This calculates the number of apnoea and hypopnoea divided by the hours of sleep, with a figure of “between” 5 to 10 being the upper end of normal (He et al., 1988).

2.7.1.1.3 Multiple latency sleep test (MLST)

It is a measure of the ability to stay awake, rarely used.

2.7.1.1.4 Flow - volume loops

Sanders et al., (1981) first reported that flow-volume loops could be helpful in identifying OSAHS. A saw-tooth pattern, defined as three or more consecutive peaks and troughs of similar configuration occurring at regular intervals of no greater than 300cc ‘during the middle half of the vital capacity in expiration, inspiration or both’, was thought indicative of variable extrathoracic airway obstruction. However, further studies using this technique (Riley et al., 1983; Tammelin et al., 1983) gave false results for OSAHS. It seems that flow-volume loops appear to correlate with the amount of fatty infiltration of the upper airway

in obese subjects-a phenomenon that is associated with OSAHS - rather than integrally part of OSAHS itself.

2.7.1.1.5 The REM sleep index

The rapid eye movement sleep index yields the number of abnormal respiratory events per time unit of REM sleep.

2.7.1.1.6 Indices of oxygen saturation measurements

One measures the number of events with saturation below a certain oxygen level (<90 per cent, 80 per cent, 70 per cent); another measures the amount of time asleep below a specific level of oxygen saturation. Generally, these indices are useful for determining the severity of the patients' initial problem and the effectiveness of the treatment or treatment chosen.

2.7.1.1.7 Index for cardiac arrhythmias

This index gives the number of arrhythmias per hour of sleep, independent of type.

2.7.1.1.8 Additional tests

Once a diagnosis of OSAHS has been established, a complete blood count may reveal secondary polycythemia. Serum electrolytes may also show bicarbonate retention due to carbon dioxide retention. Thyroid studies may be considered, to rule out hypothyroidism as an aetiological factor.

2.7.1.2 Clinical Examination

2.7.1.2.1 Oro-naso-maxillofacial region

The patient should be examined in the supine positions, as well as seated or standing. In the absence of any maxillofacial malformation, the presence or absence of dentures and other prostheses should be identified and overjet noted. An ear, nose and throat assessment is indicated to identify any obvious physical obstructions to breathing such as septal deviation, turbinate hypertrophy, and / or nasal polyp or tonsillar enlargement.

Other factors upon which our attention must focus include:

- ✓ Size, colour and covering consistency of the tongue.
- ✓ Presence or absence of pharyngeal oedema or abnormal colouring of the pharynx.
- ✓ Appearance of the soft palate and the size, length and position of the uvula.
- ✓ Aspects of the nares, including morphology and collapsibility of the nostril during inspiration whilst supine.
- ✓ Evidence of trauma,

2.7.1.2.2 Evaluation of obesity and its distribution

Height and weight are recorded, and used to calculate the subject's body mass index (BMI). This is calculated as weight (Wt) in kilos divided by the square of height (Ht²) in meters.

$$\text{BMI} = \frac{\text{Wt (kg)}}{\text{Ht}^2 \text{ (m)}}$$

The normal range for body mass index (BMI) is considered to be between 20 and 25. Subjects with a BMI of greater than 25 are overweight, whilst those whose index is greater than 30, are obese (Davies et al., 1990 and 1992; Battagel et al., 1996).

Fatty infiltration around the neck should also be investigated, and usually a simple neck circumference measurement is used to reflect upon obesity in the region of the upper airway. Neck circumference (NC), is at the level of the cricothyroid membrane. Percentage of the predicted neck size (PPNC) allows compensation for the increase in neck circumference expected to be associated with increase in height (Davies et al., 1990).

$$\text{PPNC} = \frac{100 \times \text{Neck circumference (mm)}}{[0.55 \times \text{height (cm)}] + 310}$$

Fatty infiltration of the neck will limit the ‘normal’ reflex of the mandible and tongue position during sleep, and will subsequently decrease the pharyngeal space. It is important to note that NC correlates with several later cephalographic soft - variables, and correlates better with apnoea than does BMI (Davies et al., 1992).

Distribution of atmospheric pressure upon the body tissues differs from an erect to a supine position. Therefore, the patient must be observed whilst in the supine position associated with sleep, to determine if the abdomen adopts a pear shaped

appearance, which is associated with restriction, which subsequently leads to detrimental changes in blood gases.

2.7.2 Investigations

2.7.2.1 Cephalometric radiography

Several investigators have used lateral cephalometric radiographs in an attempt to identify morphological parameters that might be characteristic of OSAHS.

2.7.2.1.1 Measurements of the face and cranium

The cranial base may be short (Bacon et al., 1988) and the cranial base angle reduced (Jamieson et al., 1986). Battagel et al., (1996) reported that the cranial base angle (Ba-SN) was significantly smaller (3.7°) in OSAHS subjects and the length of the anterior cranial base was reduced (2.4mm). This indicates a shortening of the antero-posterior dimension of the cranium and thus a more retruded face.

Rivlin et al., (1984), reported decrease in mandibular body length. Battagel et al., (1996), found reduced mandibular body length (Go-Me) by 5.9mm in the OSAHS group ($P = 0.002$). Recording this distance in the horizontal plane, to take into account variations in mandibular plane inclination, the same differences were found. Gonion to menton was 6.6mm shorter and gonion to point B 5.6mm less in apnoeic individuals.

Bimaxillary retrusion (Lowe et al., 1986a; De Berry-Borowiecki et al., 1988) or retrognathia of the mandible alone have been reported (Jamieson et al., 1986; Tsuchiya et al., 1992). Battagel et al., (1996) found that intermaxillary space length - the distance between the posterior pharyngeal wall and the lingual aspect of the lower incisor at the level of the occlusal plane - was 5.7mm shorter in

OSAHS subjects ($P=0.001$). The intermaxillary space area was also reduced, by 4.1cm^2 , indicating a lack of vertical compensation for the diminished antero-posterior development.

2.7.2.1.2 Soft tissues measurements

The soft palate is longer (Jamieson et al., 1986; Bacon et al., 1988), larger and in contact with a wider area of the tongue in OSAHS subjects (Lyberg et al., 1989). Whilst Lyberg et al., (1989) found no difference in tongue size in OSAHS subjects, De Barry-Borowiecki et al., (1988) found it to be significantly larger than in control.

Prachartam et al., (1994) concluded that although the tongue was no larger in their OSAHS group, the space in which it had to function was reduced.

2.7.2.1.3 The cervical spine and hyoid bone

Battagel et al., (1996) found that the distance from the C2 (second cervical vertebra) to a perpendicular dropped from S (sella turcica) was significantly smaller (3.6mm) in OSAHS subjects. Evaluation of the cranio-cervical angle revealed this to be increased (Solow et al., 1993).

Hyoid bone position has been found to be more inferior to normal in relation to the mandibular plane (Jamieson et al., 1986; Partinen et al., 1988).

Young JW and McDonald JP, (2004) identified a statistically significant correlation between the vertical position of the hyoid bone and the severity of (AHI) of the OSAHS condition. The vertical distance between the hyoid bone and the S (sella turcica) upon the anterior cranial base demonstrates the highest correlation with OSAHS severity (AHI). Their evidence suggest a possible

overloading of the postural system associated with efforts to maintain upper airway maintenance (reflected by hyoid bone position) as OSAHS severity (AHI) reaches extreme values (>100).

A statistically significant difference is apparent at a sella to hyoid distance of approximately 120mm, between subjects who are deemed to suffer from a mild to moderate form of the OSAHS condition and are subsequently referred for MRA management (<120), and those who are deemed to suffer from a severe form of the condition (>120). The linear measurement is proposed to be of clinical value in terms of its application in diagnostic triage and subsequent management decisions. (Young JW, McDonal JP, 2004).

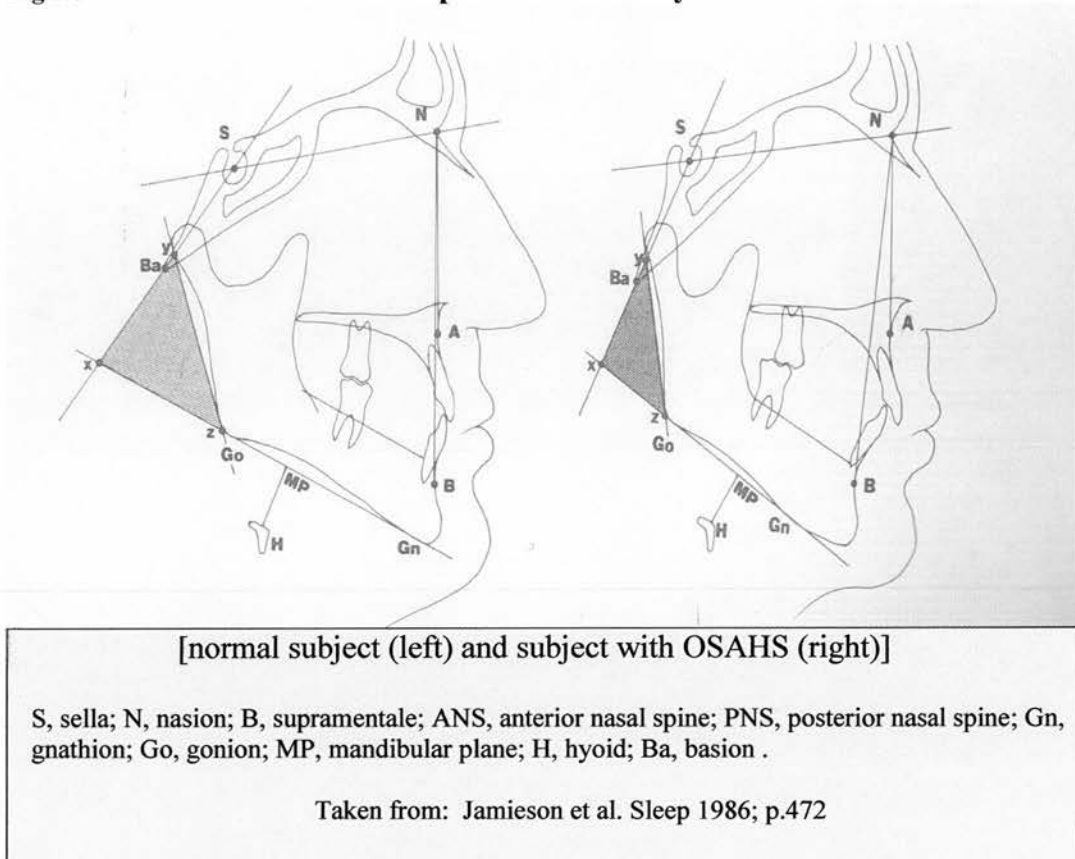
2.7.1.1.4 Oral and pharyngeal measurements

Battagel et al., (1996) found that measurements taken at all four levels of the post-palatal airway, from the upper limit of the oropharynx to the tip of the uvula, showed high degrees of statistical differences between the OSAHS and the control groups. These differences were greatest ($P=0.001$) where the soft palate was at its thickest, at the level of the lower incisor tip and at the zone of maximal protrusion of the soft palate into the airway. For all measurements, the mean airway dimensions in OSAHS subjects were approximately 66 per cent of those in the control individuals.

In the post-lingual area, by contrast, the difference in airway size between the two groups was very much smaller (Battagel et al., 1996). The dimensions of the pharynx are consistently reported to be reduced, whether the subject has been investigated in the upright or supine position (Yildirim et al., 1991).

Fig 2.5

Lateral cephalometric analysis



Highly significant craniofacial abnormalities have been found in the upper and lower pharynx in young OSAHS patients. These include significantly increased mid-facial height, narrowed middle airway space, steep mandibular plane angle, elongated pharynx and inferiorly placed hyoid bone (Johns et al., 1998). OSAHS patients were also found to have multiple sites of abnormality of both upper and lower pharynx, which may suggest that one mode of treatment such as palatal surgery alone might not be adequate treatment for these patients.

Lowe AA and Fleetham JA, (1991) evaluated whether measurements from lateral cephalometric head films are accurate predictors of these dimensional CT structures. The volumes of the tongue, nasopharynx and soft palate were accurately predicted by their cross sectional areas, but the volumes of the oropharynx and hypopharynx were not. Therefore, they suggested that

cephalogram may be useful to estimate the volume of the tongue, nasopharynx and soft palate but CT and MRI methods were superior for calculating the volume of the oropharynx and hypopharynx.

Riley et al., (1987) also recognized the limitations of using a two-dimensional radiograph to assess a three dimensional area. They found a statistically significant correlation between pharyngeal airway space measured by cephalometrics and the volume of the pharyngeal airway. Posterior-anterior cephalometry can add a third dimension to the information from lateral cephalogram to assess the shape, size and position of the turbinates and any apparent septal deviation.

Several studies have used cephalometrics to examine for anatomic differences in snoring and apnoeic subjects (Bacon et al., 1990; Nelson S, Hans, M 1997; Zucconi et al., 1992 and 1993; Maltais et al., 1991; Partinen et al., 1988). Most frequently, cephalometric radiographs of adults with apnoea were compared with radiographs of non-apnoeic adults. The tendency was for apnoeic adults to have an increased hyoid to mandibular plane (H-MP) distance, longer soft palates, a diminished sagittal cranial base dimension, and narrower posterior airways.

Few studies have investigated differences in cephalometric factors in children. A Japanese study (Shintani et al., 1992) found that children with apnoea had an inferiorly positioned hyoid. In the most severe apnoeics, the children presented with enlarged adenoids and narrow airways.

An Italian study (Zucconi et al., 1999) reported that habitually snoring children with apnoea and adenotonsillar hypertrophy had increased craniomandibular intermaxillary, lower and upper gonial angles with retropositioning, and posterior rotation of the mandible (high-angle face), together with a reduction in the nasal

posterior airway space because of enlarged adenoids. Most previous reports have used a sample of children suspected of having OSAHS, who were referred to either Sleep Disorder Centre or the Otolaryngology Department.

Randall et al., (2000) reported that there are craniofacial differences between snoring and non-snoring children. Their results manifest a significantly narrower antero-posterior dimension of the pharynx at the superior and most narrow widths. Snoring children also had a greater distance between the hyoid to the mandibular plane.

Battagel et al., (2000) studied 115 subjects. Forty-five subjects exhibited proven obstructive sleep apnoea / hypopnoea syndrome (OSAHS), 46 were simple snorers, and the remaining 24 subjects, who had no history of respiratory disease and did not snore, acted as controls. Radiographs were traced and digitised, comparisons were made of the dento-skeletal, soft tissue, and oropharyngeal features of the three groups. Differences were also sought between the snoring and OSAHS subjects. Of the hard tissue measurements, only the cranial base angle and mandibular body length showed significant inter-group differences ($P < 0.001$ and $P < 0.05$, respectively). When the airway and associated structures were examined, both snorers and OSAHS subjects exhibited narrower airways, reduced oropharyngeal areas, shorter and thicker soft palates, and larger tongues than their control counterparts did. Comparison of the two sleep disordered breathing groups showed no differences in any of the skeletal or dental variables examined. However in OSAHS subjects, the soft palate was larger and thicker ($P < 0.05$), both lingual and oropharyngeal areas were increased ($P < 0.01$ and $P < 0.05$, respectively) and the hyoid was further from the mandibular plane ($P < 0.05$).

2.7.2.2 Computer tomography scanning

Computer tomography (CT) scanning is used for imaging the upper airway. The CT scan provides soft and hard tissue images, and three-dimensional reconstruction of principal parts of craniofacial skeleton, muscles and airway space is possible. The radiation exposure limits the scope of this examination technique. As a base line, for typical effective radiological dose equivalents, an orthopantomogram delivers approximately 0.007 mSv (Equivalent to 13 days natural background radiation) whilst a CT skull delivers 2.0 mSv (Isaacson and Jones, 1994). This would make routine use of those for diagnostic purposes unethical, unless specific information, which will benefit the patient, can be obtained.

Fat deposits were seen in the collapsible segment of the pharynx in OSAHS subjects in CT studies (Horner et al., 1989).

Lowe et al., (1986) quantified the interaction between airway and tongue structures in OSAHS patients by three-dimensional reconstruction of preoperative CT slices. The majority of constrictions occurred in the oropharynx, but double constrictions were also seen in the oropharynx and hypopharynx. Large tongues appeared to cause postoperative upper airway obstructions.

2.7.2.3 Magnetic resonance imaging

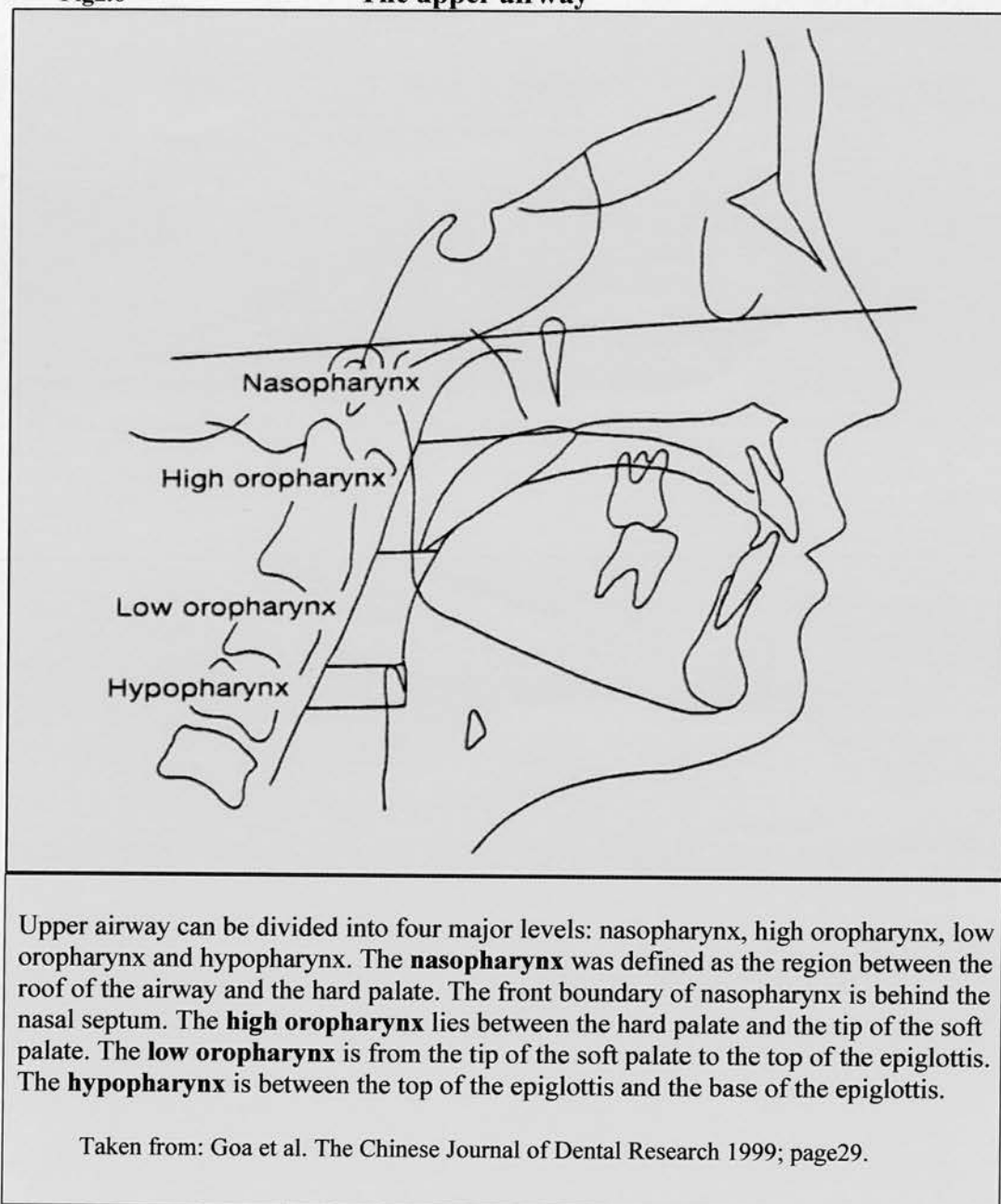
Magnetic resonance imaging (MRI) uses the property of the nuclear magnetic resonance (NMR) of hydrogen nuclei in water following excitation by a radio wave to produce a computer-derived picture of tissue. It is a non-invasive imaging technique as no ionizing radiation is used. MRI is more effective in detecting

necrotic tissue, ischaemia, malignancy and degenerative soft tissue contrast than x-ray or CT scan (William Scarfe, 1998).

MRI is an innovative technique (Hoffman et al., 1990) that produces high-resolution images without the use of ionizing radiation, making it especially well suited for soft tissue. It had been used to find small changes in the upper airway before and after nasal continuous positive airway pressure (CPAP) therapy (Abbey et al., 1989; Ryan et al., 1991).

Fig2.6

The upper airway



Xue Mei et al., (1999) used the MRI to confirm the effect of an oral appliance in the treatment of OSAHS. They found that the most enlarged part of the airway was the oropharynx during oral appliance therapy although there was also an increase in the hypopharynx. The oropharynx increased 23.7% (from 5.56mL to 6.88mL) and the entire pharyngeal size increased 13.5% (from 12.27mL to 13.93mL).

2.7.2.4 Polysonography

Overnight polysomnography is regarded as the definitive investigation for the diagnosis of OSAHS, permitting the physician to distinguish between simple snoring and true obstructive sleep apnoea hypopnoea syndrome.

The investigation is undertaken in a specially equipped sleep laboratory and designed to monitor, as non-invasively as possible, a number of variables while the subject is asleep;

- Type, frequency and duration of apnoea and hypopnoea;
- Oxygen saturation (pulse oximetry);
- Brain (EEG), heart (ECG), muscle (EMG), and eye (EOG) activity;
- Sounds (snoring and choking);
- Oral and nasal flow;
- Abdominal and thoracic respiration.

All these variables are charted, together with body position, sleep stage, and any leg or body movements. Blood oxygen saturation is under continuous observation using pulse oximetry.

Fig 2.7 Cardio-respiratory polygraphic system



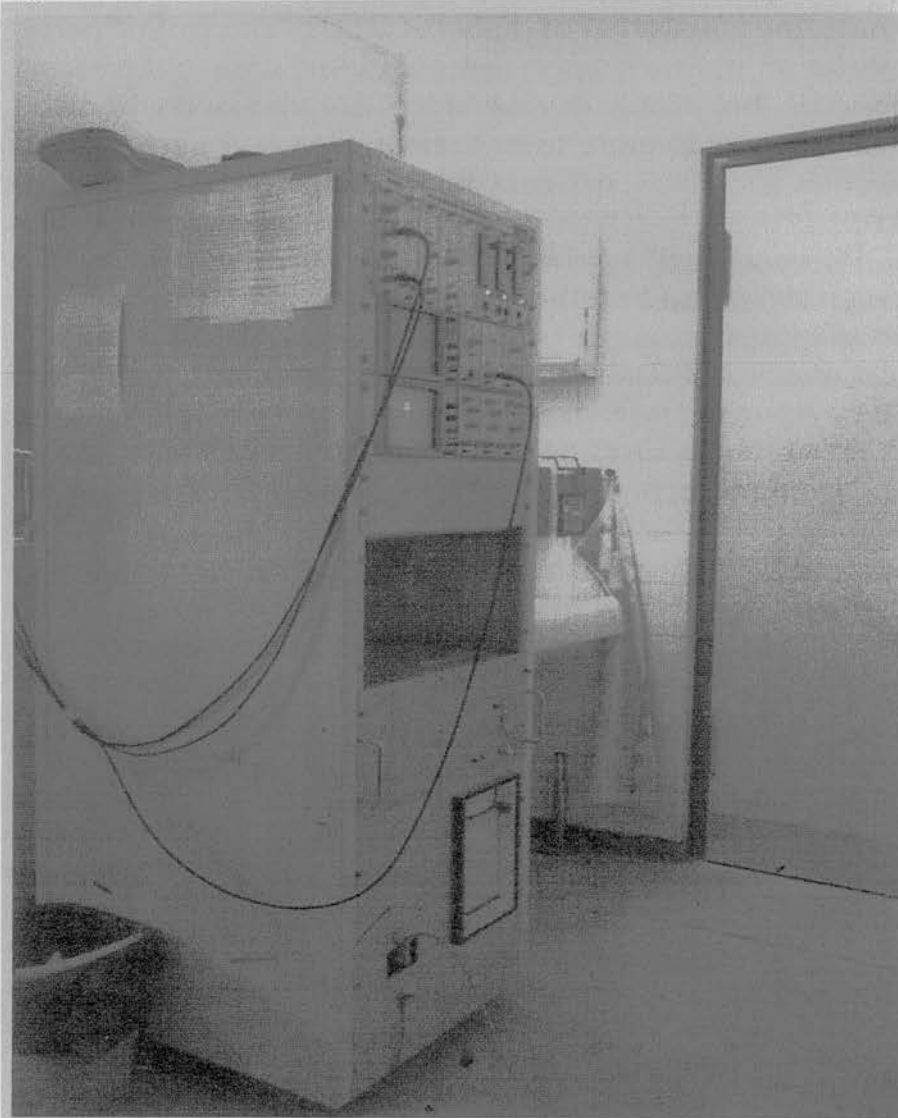
POLY-MESAM (Cardio-respiratory polygraphic system)

Early diagnosis of sleep apnoea risk patients, detection of nocturnal heart arrhythmias, imaging of periodic limb movements, differential diagnosis of breathing disorders, acoustic HR alarm, and long term records including an integrated pulse oximetry.

Taken from J Respiration; vol.64 back cover page

Fig 2.8

EISAGRAPH



EISAGRAPH (EEG Interval Spectrum Analysis)

One of the first polysomnographs developed by Drs Jung and Kuhl (O) with the engineers Tonnies and Griebel to record EEG and respiration during sleep (1967).

Taken from Respiration 1997; vol 64: pp3.

The data is fed to a bank of viewing screens in a separate room, where a technician scrutinizes them. Hard copy details of the total number and duration of the apnoeic periods, nadir oxygen saturation, time during which the oxygen saturation fell below 90% number of arousals, quantity of REM sleep. This allows not only a definitive diagnosis to be made, but also permits an evaluation of the severity of any sleep apnoea identified (Battagel et al., 1996).

Patients with OSAHS will demonstrate recurrent periods of breathing cessation with accompanying falls in blood oxygen saturation and increased abdominal and thoracic activity. In patients with simple snoring, these signs will be absent (Johal et al., 1998).

Johns MW, (1991) concluded that despite the complexity and time involved in polysomnography it is an essential procedure for the diagnosis and treatment of sleep disorders. Tan WC and Koh TH, (1991) also recognized the complexity and cost of a full polysomnographic recording.

2.7.2.5 Oximetry

Oximetry alone is often used as the first screening tool for OSAHS due to the universal availability of cheap recording pulse oximetres. They are spectrophometric devices that detect and calculate the differential absorption of light by oxygenated and deoxygenated haemoglobin in blood to produce a measurement called (SpO_2). This is an assessment of the oxygen saturation of the arterial blood arriving at the fingertip or earlobe with each pulse beat (SIGN, 2003).

Oximeters, however, have significant limitations, which must be fully appreciated before they can be used alone to diagnose clinical problems or to influence patient

management. They have an accuracy of $\pm 3\%$ between individuals and all become less reliable if tissue perfusion is poor or if coloured nail varnish is used. They can give false negative results if used on young, thin patients who generally fail to desaturate during short apnoeic or hypopnoeic episodes as they maintain their lung volumes when lying flat and their baseline oxygen saturation tends to be on the plateau part of the oxygen dissociation curve as opposed to obese individuals who desaturate easily in a similar situation (SIGN, 2003).

Oximeters are easy to use but they differ in probe design, sensitivity, sampling frequency, artefact rejection computation and averaging time. There can also be differences present in the techniques used to analyse the oximetry signals produced. Commonly employed methods include counting the number of oxygen desaturations (dips) per hour greater than an agreed value (often a 4% SpO_2 dip rate of more than 10 per hour) or alternatively the time spent during the study at less than an agreed SpO_2 level (often 90%). Thus, it can be difficult to compare results from different centres using different machines or modes of analysis (SIGN report on OSAHS, 2003).

Oximeters also register oscillations in SpO_2 when the baseline SpO_2 is low, such as in COPD, which may be confused with dips due to OSAHS. This is because at SpO_2 values below 93%, the slope of the haemoglobin saturation curve is steep and normal physiological variations in ventilation and PaO_2 produce large changes in SpO_2 . In the cheyne-stokes breathing of heart failure, oscillations in SpO_2 can be indistinguishable from those due to OSAHS (SIGN, 2003).

Oximeters, also measure heart rate and brief increases are an indirect maker of transient arousal from sleep. With each arousal the heart rate rises by about 6-10

beats per minute. Reviewing oximeter tracing with the accompanying pulse rate can provide information about sleep fragmentation (SIGN, 2003).

With overnight polysomnography blood oxygen saturation is kept under continuous observation using pulse oximetry. Cooper et al., (1991) tested the sensitivity and specificity of overnight recording of arterial oxygen saturation (Sa , O_2) in routine clinical practice and found oximetry allowed recognition of a moderate to severe sleep apnoea syndrome.

Hoffrath et al., (1991) reported short-term cyclic desaturation of oxygen could serve to indicate recurring apnoeas whereas long-lasting phasic reductions of oxygen saturation were predominantly seen in hypoventilation. They developed a computer program to differentiate cyclic and phasic oxygen desaturation. The program allowed the individual phases to be characterized in respect of gradient and duration of the decrease in oxygen saturation.

Studies using oximetry alone to diagnose OSAHS have reached widely diverging conclusions. Some found oximetry useful (Series et al., 1998; Chiner et al., 1999; and Vazquez et al., 2000) while others did not (Douglas et al., 1992; Riley et al., 1983). These differences may be explained by differences in the oximeters themselves, the analysis algorithm, and the diagnostic criteria used. Studies, which require desaturation, occur before a hypopnoea could be diagnosed, found better correlations between AHI and desaturation frequency (The Report of American Academy of Sleep Medicine Task Force, 1999). When compared with full PSG, oximetry alone showed a mean sensitivity of 87% (SE 4%, CI 36-100%) and mean specificity of 65% (SE 7%, CI 23-99%), which suggests that oximetry may be useful in selected patients with significant symptoms (AHI range 24-47%)

(Ross et al., 1999). A trained observer can diagnose OSAHS from positive oximetry traces, but false negative occur in up to a third of patients with OSAHS (Douglas et al., 1992). The limitations of oximetry need to be clearly understood, namely, oximetry can positively diagnose OSAHS but cannot be used to exclude OSAHS (SIGN, 2003).

- A normal oximetry tracing does not exclude OSAHS.
- The characteristic oximetric tracing in OSAHS is a sawtooth pattern, however care should be taken interpreting this pattern as it may also appear in patients with COPD or congestive heart failure.
- Automated analysis is available for many sleep systems but the validity of this should be checked by an experienced operator.

2.7.2.6 Fluoroscopy

Fluoroscopy has been employed in investigations of upper airway obstruction (Suratt et al., 1983) and to study adaptive patterns of behaviour in the oropharyngeal complex (Vig PS and Cohen AM, 1974). The dynamic effect of mandibular advancement on the adaptive patterns of behaviour of tongue, soft palate and airway have been described in a pilot study using high resolution fluoroscopy in the conscious, supine, OSAHS subject (L'Estrange et al., 1996). This indicated a wide range of individual variation in the dimensional changes of the post-palatal and post-lingual airways in response to mandibular protrusion.

2.7.2.7 Acoustic reflectance technique

Acoustic pulse reflectometry is a relatively recent technique, which allows non-invasive measurement of human airways. The technique consists of guiding an

acoustic impulse through the patients' mouth and into the airway. The resulting reflectance or 'echo' is been analysed allowing a reconstruction of the area-distance function.

The non-invasiveness of the technique offers significant advantages over the established methods of cephalometric radiographs and CT scanning. The technique can be used for investigating ENT problems and OSAHS (Marshall et al., 1991). Airway obstructions can be confirmed by acoustic reflectance techniques (Rivlin et al., 1984). These researchers also documented, with acoustic reflectance technique, a widening of the pharyngeal cross sectional area in one patient who lost 68 kg in weight suggesting that peripharyngeal fat deposits may contribute to OSAHS.

2.7.2.8 Fibroptic and nasal endoscopy

In this technique the nasal cavity and pharynx is anaesthetized topically and the fibroptic pharyngolaryngoscope is introduced through the nose to examine the nasopharynx, oropharynx, hypopharynx and larynx in sequential steps. The positions of the soft palate, base of the tongue and lateral pharyngeal wall are noted and photographed. The base of the tongue position and its movement on protrusion of the mandible is noted. The larynx is also examined for deformities or masses (Riley et al., 1987). Nasendoscopy allows visualization of the entire airway and obvious areas of narrowness will be detected.

One research group (Croft et al., 1990) for observing the pharyngeal airway in infants and young children, using a flexible endoscope assessed nasal endoscopy. The endoscopy performed under light anaesthesia revealed the site of the obstruction in all cases examined.

2.7.2.9 Nasal capnography

Measures of end-tidal carbon dioxide concentration proved to be a very insensitive index of the degree of obstruction (Smith et al., 1993).

2.7.2.10 Questionnaires

Three studies were identified comparing questionnaires sampling in OSAHS patients to full PSG. These reported a mean sensitivity and specificity of only 42% and 68% respectively.

Questionnaires are useful in the initial assessment of the potential OSAHS patient, but by themselves, cannot make the diagnosis (Johns MW, 1991; Shelton et al., 1993; Pouliot et al., 1997).

2.8 MANAGEMENT

The management of OSAHS depends on the severity of symptoms, the magnitude of clinical complications and the aetiology of the upper airway obstruction. The treatment of OSAHS is divided into non-surgical and surgical procedures:

NON - SURGICAL TREATMENT

- Elimination of aggravating factors
- Weight reduction
- Training
- Pharmacological therapy
- Electrical stimulation of the upper airway
- ENT assessment plus any necessary treatment
- Continuous positive airway pressure
- Intra-oral appliances
- Nasal-valve dilator

SURGICAL TREATMENT

- Tracheostomy
- Nasal surgery
- Pharyngeal surgery (Uvulo-palato-pharyngoplasty)
- Maxillofacial surgery
- Tonsillectomy and adenoidectomy
- Tongue reduction
- Bariatric surgery

2.8.1 Non-surgical treatment

2.8.1.1 Elimination of aggravating factors

As was mentioned in the pathophysiology, a number of factors may aggravate OSAHS. Co-existing chronic obstructive airway disease, asthma, and hypothyroidism are known medical conditions, which will make OSAHS worse. Adequate therapeutic control of these factors is therefore important in management. The intake of alcohol and other CNS depressants including sleeping tablets, will make the airway more prone to collapse during sleep and therefore cutting down on one's alcohol intake particularly during the evening, is sensible, if not always palatable advice (Battagel et al., 1996).

The SIGN report (2003) on OSAHS advised the following:

- Patients who smoke should be advised to stop.
- Alcohol and sedatives or sleeping tablets should be avoided.
- Non-sleepy snorers should be discouraged from sleeping on their back.

These measures may suffice in simple snorers or in those with very mild OSAHS and few symptoms but most patients with OSAHS need additional treatment.

A Cochrane review of lifestyle modifications for OSAHS is identified no randomised clinical trial (RCT) evidence supporting their use and concluded that any decision to institute such interventions should not delay the institution of therapies of proven effectiveness, such as CPAP (Shneerson J and Wight J, 2002).

2.8.1.2 Weight reduction

Obesity exacerbates OSAHS; fatty deposits both subcutaneously and in the pharyngeal wall lead to further narrowing of the oropharynx, encouraging its occlusion once the subject is supine. Because many OSAHS sufferers are obese, weight loss is frequently suggested. This change in life style is far from easy to accomplish and many individuals are insufficiently motivated. For those who are committed, dietary advice should be provided. Once weight has been lost, regular exercise is easier and this is in the subject's overall medical interests. However, although the subject may feel fitter and less lethargic when his weight is within normal limits, his apnoea may not show a parallel improvement (Battagel et al., 1996).

Rajala R et al., (1991) associated OSAHS with morbidly obese patients, and showed that treatment with a dietary regimen significantly improved or occurred 55% of the patients with mean reduction in BMI of 27%.

The SIGN report (2003) on OSAHS stated that:

- Weight loss should be encouraged in all patients with obesity contributing to their OSAHS.
- Attempt at weight loss should not delay the initiation of further treatment.
- Weight loss should also be encouraged as an adjunct to CPAP or intra-oral devices as it may allow discontinuation of therapy.

2.8.1.3 Training

A pillow attached to the sleeper's back by a belt around the waist or a tennis ball sewn into the pyjama top at the midback level are probably the two most

commonly employed devices. Posture alarm could be tried (Cartwright et al., 1991).

Rosalind et al., (1985) trained 10 known OSAHS patients to avoid the back sleep position by wearing a gravity-activated position monitor / alarm on the chest. This device emits an auditory signal if the patient remains supine for more than 15 seconds. They found the number of apnoeic events was significantly reduced, as well the number of episodes of significant O₂ desaturation.

2.8.1.4 Pharmacological therapy

The evidence base to support pharmaceutical treatment as an effective therapeutic option is small. The main systematic review of pharmacotherapy concluded that no medication demonstrated a consistent response (Hudgel DW and Thanakitcharu S, 1998; Smith et al., 2002). Pharmaceutical agents may on occasion provide some relief of symptoms associated with OSAHS. Generally, the aim of such therapy is to increase glossopharyngeal neurologic activity or to decrease REM sleep.

There is some evidence to suggest that the addition of alerting drugs, such as modafanil, may have a small beneficial effect on sleepiness in some patients who remain sleepy despite good CPAP compliance. However, they may decrease CPAP use and longer term studies of their value and risks are needed (Kingshott et al., 2001). There is no evidence to suggest that they could be used as an alternative to CPAP and they are not a substitute for careful attention to improving CPAP comfort and efficacy.

Medications most frequently prescribed for the treatment of the condition include protriptyline and theophylline. Unfortunately, these drugs are unsuitable for many

subjects and of unproven efficacy. The search for a more appropriate alternative is ongoing.

Pharmacological therapy should not be used as first line of therapy for OSAHS (SIGN report on OSAHS, 2003).

2.8.1.4.1 Protriptyline

Protriptyline (a non-tricyclic antidepressant), the most commonly used and the most studied. It may be associated with a mild reduction in apnoeic episodes (Findley LJ et al., 1985). It was initially introduced as a treatment for OSAHS based upon its ability to reduce the frequency of apnoeic events and oxygen desaturations during non-REM sleep, while at the same time suppressing REM activity (that stage during which the apnoeas tend to last the longest). Later investigations revealed an additional benefit of specifically increasing tone of the upper airway musculature (Borona et al., 1984). Unfortunately, severe anticholinergic side effects are evident in approximately half of the subjects taking the drug (Mulloy E and Nicholas WT, 1992).

2.8.1.4.2 Theophylline

Mulloy E and Nicholas WT (1992) have investigated the effect of theophylline on OSAHS patients, and noticed a decrease in the total number of apnoeas and hypopnoeas, as well as in AHI, but at the same time, they found that sleep quality deteriorated significantly. Unfortunately, there appears to be no reliable means of predicting which patients are likely to benefit from theophylline, although it is thought that it may be those with mild disease.

2.8.1.4.3 Oxygen administration

Nocturnal hypoxaemia in sufferers of OSAHS may contribute to the development of cardiopulmonary morbidity. Thus, prevention of hypoxaemia is a worthwhile therapeutic goal in these patients. Studies to date indicate that providing supplemental oxygen during sleep is not sufficiently effective in reducing the frequency of apnoea and increasing daytime alertness to stand alone as therapy for most patients (Watt JG et al., 1943).

2.8.1.5 Electrical stimulation of the upper airway

Preliminary studies indicate that electrical stimulation of the submental muscle (genioglossus), which act as upper airway dilator, will enhance luminal patency and reduce the number of obstructive apnoeas (Miki H et al., 1989).

2.8.1.6 ENT assessment plus any necessary treatment

This is important, as airway, obstruction may originate in, or be complicated by, obstruction in the nose or nasopharynx. Both visual and nasendoscopic examinations should be carried out. Septal deviation, turbinate hypertrophy, nasal polyps, or tonsillar enlargement may be found and their correction indicated. In addition, nasendoscopy also allows visualization of the entire airway and obvious areas narrowness will be detected.

2.8.1.7 Continuous positive airway pressure (CPAP)

CPAP is the so-called 'gold standard' of treatment of OSAHS, developed by Colin Sullivan, in Australia in 1981. It provides dramatic relief of symptoms and ensures airway patency during sleep (Sullivan CE et al., 1981) by elevating the

pressure in the oropharynx. A continuous stream of air under low pressure is filtered and delivered to the pharynx via a nasal mask. This constant flow is sufficient to prevent the airway from collapsing regardless of the position of the subject, but not enough to prevent expiration. The mask must fit firmly round the nose and to secure it, a head cap and retaining straps must be worn. CPAP should be in place for 4 to 6 hours per night, seven nights a week (Engleman et al., 1994; Battagel et al., 1995).

A distinctive feature of CPAP therapy is the immediate and dramatic response. Typically, within moments of its application, the patient begins to exhibit long periods of uninterrupted sleep, marked rebound in stage 3 to 4 NREM sleep occurs, and both the frequency and duration of this stage sleep increase dramatically. This rebound continues over a number of nights, until, by the seventh to the tenth night, distribution and reusability generally return to normal levels. The daytime function of subjects is often transformed and while the loss of daytime somnolence is the most characteristic feature, all other symptoms of OSAHS may also be reversed.

Whilst generally extremely effective, it is appreciated that CPAP is often a difficult device to tolerate. The pump delivering the air stream is noisy, making a constant 'humming' reminiscent of an air-conditioning unit. The anti-social nature of the mask and the headgear coupled with cumbersome and sometimes impractical nature of the device are thought to be of significant importance with regard to its acceptance and compliance.

Long term compliance with CPAP has been estimated at between 60% and 70% (Battagel et al., 1996).

Figure 2.9 Continuous positive airway pressure (CPAP)



Taken from University of Chicago Sleep Medicine website, www.sleepmed.bsd.uchicago.edu

While nCPAP provides air stream pressure sufficient to exert a splinting effect upon the upper airway, the air pressure is insufficient to prevent periodic expiration. This addresses the complaint voiced by a number of OSAHS subjects, that they find expiration difficult with conventional CPAP. In situations where persistent difficulty with expiration is reported, alternative approaches include the use of Bilevel CPAP (BiCPAP), which utilizes a second tube allowing a separate channel for expiration, and a device incorporating ramp type feature whereby pressure does not increase until the patient is already asleep.

Interestingly, investigations have revealed no increase in compliance with these alternatives (Battagel JM et al., 1995).

A major concern with nCPAP as a therapeutically effective method of treatment of OSAHS centres upon the long-term compliance of the subject. The use of the device in the longer-term requires considerable patient commitment, and the patients who suffer most from the symptoms associated with the OSAHS condition are more likely to be consistent with its use. The overall long-term compliance has been estimated to be between 50 and 70% (Walldhorn RE et al., 1990; Westbrook PR et al., 1990; Hofstein V et al., 1992; Grundstein RR, 1995), though this figure has been found to drop to approximately 30% for mild cases (Rolfe I et al., 1991). Interestingly, when studies have been performed in which the actual use of CPAP is monitored 'covertly', compliance has been found to be significantly less than was self reported by the patients (Rauscher H et al., 1991).

The reported benefits of nasal CPAP are:

- improved quality of life;
- improved daytime cognitive function;
- reversal of daytime symptoms-in particular, sleepiness;
- elimination of snoring and other night-time symptoms;
- long term improvement in cardiovascular function, with reduction in blood pressure;

Major side effects of CPAP use (eg. significant epistaxis, paranasal sinusitis) are rare, but minor side effects (irritation related to the mask, nasal bridge sores

(Sjoeholm et al., 1994), nasal congestion, dryness or excessive rhinorrhea, upper respiratory tract infections, abdominal bloating, discomfort, noise, chest pain, and feelings of claustrophobia) are common. Intensive efforts can achieve CPAP uptake of up to 95% (McArdle et al., 1999) and an average nightly use of three to five hours (Engleman et al., 1996; Richards et al., 1996). Nasal symptoms are usually due to mouth leaks causing high flows of cool air through the nose. Attempts should be made to reduce these, using chin straps or full face mask (SIGN report, 2003). In a few patients, nasal corticosteroids can be useful (SIGN report, 2003). A heated humidifier may help to improve comfort and compliance (Massie et al., 1999).

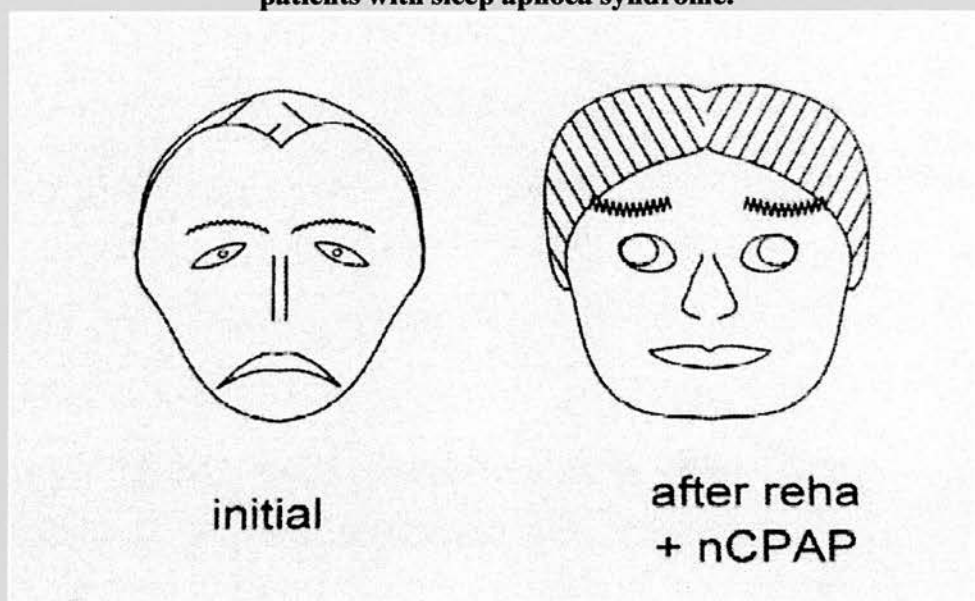
The Scottish Intercollegiate Guidelines Network report (2003) for OSAHS, which is endorsed by the British Thoracic Society, has recommended the following:

- CPAP should be the first choice therapy for patients with moderate or severe OSAHS that is symptomatic to require intervention.
- Bi-level ventilation should not be used routinely in OSAHS but should be reserved for patients with ventilatory failure.
- Persistent low CPAP use (less than two hours per night) over 6 months, following efforts to improve patient comfort, should lead to review of treatment.

The SIGN (2003) report for OSAHS also recommended that, CPAP therapy should not be abandoned without:

- ✓ The attention of a trained CPAP nurse / technician.
- ✓ A titration study / use of autotitrating CPAP to troubleshoot problems.
- ✓ The use of heated humidification.

Fig 2.10 Multivariate representation of subjective physical and mental condition of patients with sleep apnoea syndrome.



Taken from Fischer J and Raschke F. J Respir 1997; vol.64: pp41.

2.8.1.8 Intra-oral appliances

- **Mandibular repositioning appliances**

- Nocturnal airway patency appliance (NAPA)
- Sleep and nocturnal obstructive apnoea reducer (SNOAR)
- Snore guard
- Jasper Jumper

- **Tongue repositioners**

- Tongue retainers

Tongue retaining device (TRD).

Tongue locking device (TLD).

- Tongue posture trainers

Tepper oral proprioceptive stimulator (TOPS).

Tongue positioner and exerciser (TPE).

- **Soft palate lifters**

- **The equalizer**

- **Magnetic appliances**

2.8.1.8 Intra-oral appliances

Since Pierre Robin first described his monobloc appliance in 1902 for the treatment of glossoptosis (tongue falling back and occluding the airway) in infants, several appliances have been appeared for the treatment of upper airway obstruction. The term 'oral appliance' is used as a generic term for devices inserted into the mouth in order to modify the position of the mandible, the tongue and other structures in the upper airway for the purpose of relieving snoring or sleep apnoea.

There are five basic categories of dental appliances used in the treatment of OSAHS: the mandibular repositioning appliances, the soft palate lifters, the tongue repositioners, the equalizers and the magnetic appliances.

2.7.1.8.1 Mandibular advancement appliances (splints)

Like CPAP, Mandibular Advancement Appliances (MAA) are a non-invasive and therefore reversible form of treatment, and worn only during sleep. The rationale for the use of (MAA) is that they may increase the size of the pharyngeal airway by drawing the tongue and soft palate forwards, and thus maintain its patency during sleep.

Lui et al., (2000) selected twenty two patients who were confirmed with a diagnosis of obstructive sleep apnoea based on initial nocturnal polysomnography. The patients were fitted with a mandibular repositioner designed to hold the mandible antero-inferiorly. Six months later, an outcome polysomnographic study was undertaken for each patient with the appliance in place. Lateral cephalometric radiographs in the upright position were also obtained before and after 6 months of treatment. The apnoea hypopnoea index

decreased in 21 of the 22 patients with the appliance in place. The mean respiratory disturbance index of the 22 patients decreased significantly from 40.3 to 11.7 events per hour ($P < .01$). Some 59.1% of subjects were considered a treatment success with follow-up respiratory disturbance index < 10 events per hour. The mean minimum blood oxygen saturation level during sleep also improved significantly from 73.4% to 81.3% ($P < .01$).

Mechanism of action

The mechanism by which these appliances work appears simple. The MAA prevent the tongue collapsing against the posterior pharyngeal wall nocturnally. This achieved by mechanical means in that the origin and insertion of genioglossus is at the hyoid bone and mandibular symphyseal region respectively. Thus, by advancing the mandible, the tongue is held in a more anterior position nocturnally, hence increasing the airway space.

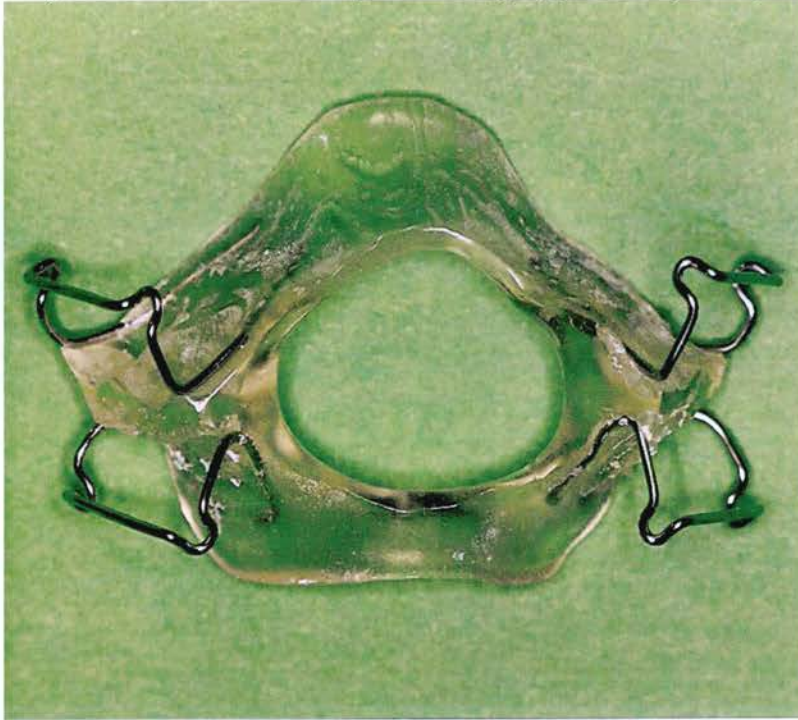
A second consideration given by Lowe et al (1994) is that, in man, voluntary passive opening of the mandible produces definite enhancement of genioglossus EMG through activation of receptors located in the temporomandibular joint. Because the contraction of the genioglossus opens the airway, so airway obstruction is prevented. It has also been proposed that the increased vertical dimension achieved with these appliances acts to increase tonicity of the tongue, thereby reducing the risk of airway occlusion (Lowe et al., 1990).

Appliance Design

The mandibular repositioning appliance has many different variations. It is typically constructed of clear acrylic resin, together with retentive Adams' clasps.

The guideline for the optimal amount of forward movement is between 50% and 75% of the patient's maximum protrusive distance. This forward position can be maintained by use of a one-piece or fixed appliance that holds the maxilla and mandible together, with retention being provided by clasps, acrylic or thermoplastic polymer. Protrusion cannot be achieved without some concomitant opening and it is important that appliances do not rotate the mandible downwards and back (Lowe et al., 1994). An important feature of this appliance is that anterior air holes are necessary to allow oral respiration, especially for those with restricted nasal airflow. Common used designs include the cribbed activator (Bonham et al., 1988), vacuum-formed devices, the Nocturnal Airway Patency Appliance (Soll et al., 1985) and the Sleep Nocturnal Obstructive Apnoea Reducer (Viscomi RT al., 1988).

Fig 2.11 Mandibular Repositioning Appliance (MRA)



MRA (Frontal view)

It is a design of mandibular advancement appliance used within the Orthodontic Dept. Victoria Hospital, Fife, Scotland.

2.8.1.8.1.1 Nocturnal airway patency appliance (NAPA)

Soll et al., (1985) described a modified activator that advanced the mandible 6mm anteriorly and 9mm inferiorly for one patient and significantly reduced the AHI. The appliance has eight Adams clasps with overlapping acrylic on the facial and lingual surfaces of the teeth. It is designed to protrude the mandible about three quarters of the distance between centric occlusion and full protrusion. The mandible is opened vertically just enough to permit an airway between the incisors. The NAPA rigidly stabilizes the mandible in both the horizontal and vertical dimensions. The effects of the NAPA in reducing the AHI have been documented in subsequent studies (George PT, 1987 and 1989).

2.8.1.8.1.2 Sleep and nocturnal obstructive apnoea reducer (SNOAR)

The SNOAR open airway appliance is an acrylic mandibular advancement appliance that advances the mandible 6 to 9mm and opens it vertically 17mm or more.

Viscomi et al., (1988) reported in his study that, the mean AHI was reduced from 45.5 to 9.7 and snoring was absent after the SNOAR appliance was inserted.

2.8.1.8.1.3 Snore guard (Dental orthosis)

This prefabricated appliance positions the mandible 3mm behind the maximum protrusion with 7mm opening. It covers only the anterior teeth and is lined with a soft polyvinyl for patient comfort. It is easy to fit and adjust directly on the patient and appears to be well tolerated.

In two initial studies (Schmidt-Nowara et al., 1988 and 1991) snoring was decreased significantly or completely eliminated. Later reports (Dushell et al., 1991; Menn et al., 1992) found a significant decrease in AHI, particularly among mild apnoea sufferers.

For patients with active bruxism and / or those who feel restricted by the rigid fixation of their jaws with the one-piece design, an alternative, more ideal, design involves constructing separate maxillary and mandibular appliances. Connecting the upper and lower appliances is accomplished with inter-arch elastics and buccal tube and rod attachments (e.g. Herbst appliance, Jasper Jumper), or a single hook and latch in the anterior region (e.g. Thorton Adjustable Positioner). The objective of this design is to restrict all retrusive movements while still allowing the patient to move the mandible forward and side to side, as well to open the mouth if necessary.

An additional advantage of the two-pieces appliances is the ability to systematically pinpoint the exact mandibular position that benefits each patient the most. It is possible to start at 50 % of maximum protrusion at the first appointment and then gradually advance the mandible until all signs and symptoms completely disappear. On the other hand, these appliances, because of their construction, may be difficult for the subject to manage.

The Herbst Mandibular Advancement Splint is a justifiable option in selected subjects with sleep-related breathing disorders. (Shadaba et al., 2000).

2.8.1.8.1.4 Jasper jumper and twin block

Only one preliminary evaluation of this appliance for the treatment of OSAHS has been completed (Coghlan MSc, 1990), in which 11 subjects with varying degrees of OSAHS were evaluated. Seven of the 11 subjects tested before and after appliance, insertion had reduced AHI values, but there were no significant differences. Even after vertical elastics were added, only half of the subjects tested showed a reduced AHI. This appliance may be more easily tolerated than the more rigid mandibular advancement appliances, but additional studies with varying mandibular vertical and anteroposterior positions are required to verify its usefulness.

2.8.1.8.2 Tongue repositioners

2.8.1.8.2.1 Tongue retainers

2.8.1.8.2.1.1 Tongue retaining device (TRD)

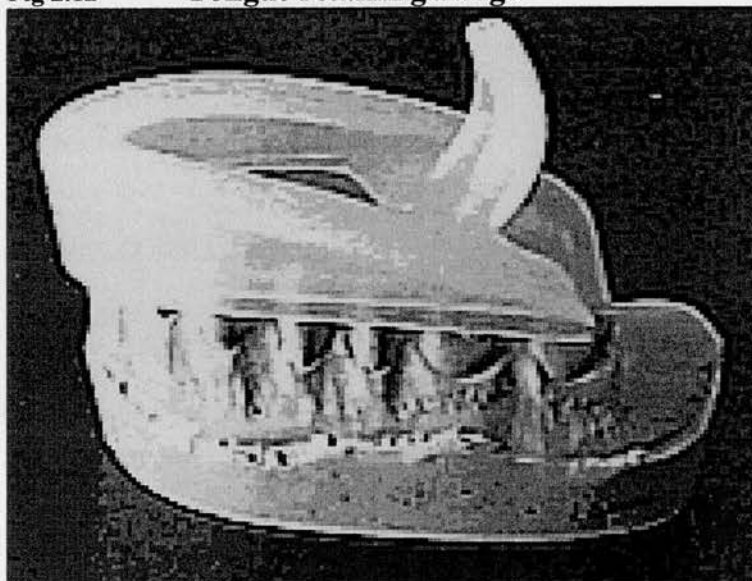
The TRD is designed to reposition the tongue forward during sleep; thereby reducing the risk of obstruction at this level (Cartwright et al., 1982). The device

secures the tongue by means of negative pressure in a soft plastic bulb; a flange, which fits between the lips and teeth, holds the device and tongue anteriorly in the oral cavity. It should be noted that this appliance also modifies mandibular pressure at least by forward rotation. The TRD has been fabricated from dental impressions, but a prefabricated version suitable for moulding to the patient's teeth in the clinic is now available; it can also be used in edentulous patients. For those patients with blocked nasal passages a modified TRD with lateral airway tubes is also available. The disadvantage of the TRD is that the tongue is not always held forward because surface adhesion of the tongue in the bubble is lost after time, and the patient must then awaken and relocate the tongue into the bubble. An aesthetic drawback is that the tongue must slightly protrude between the teeth.

The TRD is the only appliance that has been studied in various body positions and in conjunction with other forms of therapy (Cartwright et, al., 1982). The TRD appears useful, either alone or in conjunction with other treatments, for improving patients with a wide range of apnoea severity, provided that the apnoea is more severe in the supine position and the patient's weight is not greater than 50 per cent of the ideal (Lowe A, 1994).

Compared to the most commonly performed CPAP, the TRD is the more easily tolerated and has fewer long-term compliance problems.

Fig 2.12 Tongue retaining flange



Device with tongue-retaining flange

(Shown upside down)

The flange is intended to hold the tongue out of the airway. The patient cannot swallow when using this type of device. In addition, the flange can cause obstruction of small upper airways (a common finding in OSAHS). Many consider these devices unsafe.

Taken from Vancouver Sleep Centre web site; www.sleep-breathing.bc.ca/mandib.htm

2.8.1.8.2.1.2 Tongue locking device (TLD)

This patent appliance is simple preformed elastic available in small, medium and large sizes that provides a cavity for the tongue and holds it forward with a self-created vacuum during sleep. Lateral breathing holes assist airflow if nasal obstruction occurs. The TLD is simple to fit directly on patients and is inexpensive.

Prinsell et al., 1992 studied 10 OSAHS subjects and found that five individuals had a reduction in AHI and five subjects became worse.

2.8.1.8.2.2 Tongue posture trainers

2.8.1.8.2.2.1 Tepper oral proprioceptive simulator (TOPS)

This appliance is fitted to the maxillary arch with a posterior tongue extension held inferiorly with an elastic band. An anterior padded bar lingual to the incisors is included to direct correct tongue placement. According to Dr. Tepper: its prime use is for those patients who snore, have apnoea, have problems of abnormal tongue posture and / or function and for those who have loss of muscle tonus of the soft palate and pharynx. All these abnormalities are corrected by proprioceptive means wherein the receptors are stimulated by the hinged portion of the appliance resting on the dorsum of the tongue. By increasing the resistive force of the elastics, we can strengthen dorsal muscles of the tongue. Thus by correct repositioning of the entire tongue to the hard and soft palate; it is my concept that we can increase airway space. Published data on its effectiveness for the treatment of OSAHS are not yet available.

2.8.1.8.2.2.2 Tongue positioner and exerciser (TPE)

The tongue positioner and exerciser is a custom-made appliance that has been used to treat snoring. Patients are trained to position the tongue above the ramp; according to the inventor, this 'retrains the tongue and lip musculature to be in the proper rest and saliva swallowing position'. Published results before and after appliance insertion are not yet available.

2.8.1.8.3 Soft palate lifters

Paskow et al., 1991 invented the adjustable soft palate lifter (ASPL). The appliance is designed to lift the soft palate gently and prevent it from vibrating in

the air passage during sleep. The ASPL consists of a maxillary removable appliance with two Adams clasps on the molars and an acrylic button that extends distally to the midpoint of the soft palate. Patients who gag are 'desensitised' with palatal exercises that consist of contact with the end of a spoon or toothbrush five or six times a day. Paskow claimed 60 per cent success rate for snoring but felt the appliance is not indicated for the treatment of OSAHS. However Marklund et al., (1996) found that the soft palate lifters were insufficient for the treatment of snoring.

2.8.1.8.4 The equalizer

This appliance is introduced by Haze in 1987; it is constructed of vinyl material and repositions the mandible in a position of "neuromuscular balance" as determined by a myomonitor, a transcutaneous electroneural stimulator.

2.8.1.8.5 Magnetic appliances

Very recently, a magnetic appliance has been used for treatment of snoring patients with or without obstructive sleep apnoea (Bernhold et al., 1998). A magnetic appliance may be more effective than the conventional 'passive' functional appliance, because the magnet forces prevent the closing by providing direct and continuous mandibular advancement. Long-term evaluation of the treatment results is needed before routine use of the magnetic appliance in apnoea patients.

The Scottish Intercollegiate guidelines Network report (2003) on OSAHS which is also endorsed by the British Thoracic Society concluded that:

- Intra-oral devices are an appropriate therapy for snorers and for patients with mild OSAHS with normal daytime alertness.
- Intra-oral devices are an appropriate alternative therapy for patients who are unable to tolerate CPAP.
- The use of intra-oral devices should be monitored following initiation of therapy to allow device adjustment and assessment of OSAHS control and symptoms.

Advantages of Oral Appliances

The advantages of oral appliance therapy are simplicity, reversibility and cost effectiveness. It may also become the primary treatment in patients who are unable to tolerate nasal CPAP or who are poor surgical risks. Most patients readily accept it and it can even supplement other treatments in the small percentage of cases in which the dental devices alone do not bring sufficient relief of symptoms.

Disadvantages of Oral Appliances

Excessive salivation and transient discomfort in the muscles of mastication for a brief time after awakening are commonly reported with initial use and may prevent early acceptance of oral appliances (Schmidht-Nowara et al., 1991; O'Sullival et al., 1995), but with regular use and adjustment of fit, these symptoms subside. Pantin et al., (1999) reported that hypersalivation and teeth / gum discomfort are the early side effects but usually decline if patients are able to persevere with Intra-Oral Devices (IOD) use.

Later complications might include TMJ discomfort and changes in occlusion, and have been reported as reasons for discontinuing treatment (Schmidht-Nowara et al., 1995). To prevent these changes the design should use full-arch occlusal coverage to tie all the teeth firmly together (O'Sullivan et al., 1995). This simply means that the appliance will no longer fit if any individual tooth moves.

However, (Schmit-Nowara et al., 1995) suggest that TMJ dysfunction and occlusal changes are relatively uncommon occurrences, but the long-term risk of these complications is not well defined.

There was one report of TMJ problems after a period of 15 months wear, which settled after adjustment of the splint (Joha A and Battagel J, 1999).

Efficacy of Oral Appliances

Reported success rates vary, as do the authors' criteria for its achievement. If a reduction in the number of apnoeic events of 50% or greater is adequate, then success rates are as high as 87%, as reported by Clark et al., (1993). The most comprehensive review of 20 publications, reporting the effects of oral appliances on OSAHS (Schmit-Nowara et al., 1995), showed an improvement in average AHI with a dental appliance. Success was equated with fewer than 10 apnoeic events per hour. When statistics were provided, the decrease in AHI was always significant ($P < 0.05$), and the mean AHIs before and with treatment were 42.6 and 18.8 respectively, an average reduction of 56%. An improvement in oxygen saturations was also noted, and the time of sleep with oxygen saturation $< 90\%$ was reduced from 4.4% to 3.1%.

Two recent prospective crossover trials (Ferguson et al., 1997; Bennet et al., 1998) compared mandibular repositioning appliances and continuous positive airway pressure (CPAP) in patients with mild to moderate obstructive sleep apnoea. The success rate with the oral appliance was 55% in both trials, though the improvement in AHI reduction was greater when the continuous positive airway pressure was used.

A meta-analysis of patients' treatment preference (CPAP and IODs) in three crossover studies in mild to moderate OSAHS showed a significant patient preference for IODs (OR 9.5, 95% CI 4 to 21), despite lesser nocturnal efficacy for breathing pauses (-7 per hour, 95% CI -10 to -5) (Wright et al., 2002). This was not confirmed in a later study (Engleman et al., 2002). Patients' preference for IODs is important, but it is not known if this means that they feel symptomatically better when using IODs or whether they find the concept of an unobstructive intra-oral device preferable to using obstructive CPAP device (SIGN, 2003).

One group has compared the effectiveness of IOD against UPPP in a parallel group, longitudinal follow-up study, with the latest report at four years post-randomisation (Walker-Engstrom et al., 2002). In this, 72 of 95 patients with mild to moderate OSAHS have returned for polysomnography, which showed large effect size (>1.0 SDs) significantly favouring IOD over UPPP for improvements in AHI and desaturation index, but no significant differences in snoring duration between treatments.

Cost

A formal survey of the cost devices and services has not been performed for oral appliances. The production cost of the device varies depending on whether a dental laboratory is required for custom fitting or prefabricated unit can be adapted in the clinician's practice. When cephalometric radiographs or other airway studies are performed as part of the procedure, the cost increases accordingly.

It is unclear whether continuous positive airway pressure (CPAP) or intra-oral devices (IODs) have the greater cost effectiveness and the answer may vary with OSAHS severity. The basic cost of many IODs is less than the cost of a CPAP machine. Some adjustable IODs are more expensive than CPAP, especially when the cost of multiple dental visits to adjust the IOD are included (SIGN, 2003).

Compliance

Data on long-term compliance is limited in number and is based on patient reports. The experience with nasal CPAP, however, indicates that self - reports may significantly overestimate objectively determined actual use (Rauscher et al., 1991). Overall compliance rates vary from (50 to 100%) in different studies and may be related to the length of follow - up (Schmidt-Nowara et al., 1995). The reasons for discontinuing appliance use include the side effects and complications noted above and lack of efficacy.

2.8.1.9 Nasal-valve dilator

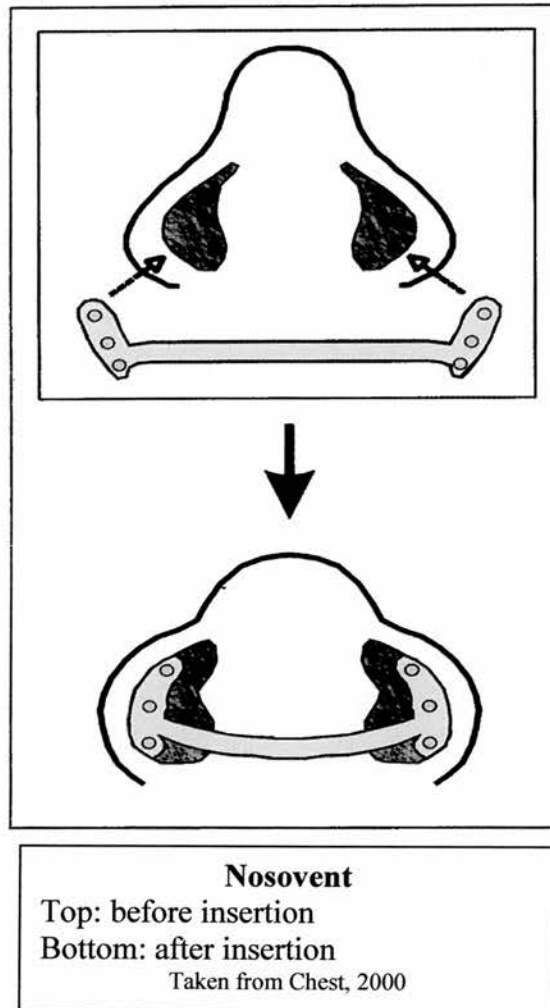
Increased nasal resistance may induce sleep-related breathing disorders and disturbed sleep (McNicholas et al., 1982; Millman et al., 1996; Zwillich et al.,

1981). It has been shown that several devices, including nasal-valve dilators (Nozovent; Prevancure AB; Västra Frölunda, Sweden), reduce nasal resistance and improve nasal breathing (Lorine et al., 1998; Metes et al., 1992). The Nozovent device consists of a plastic bar that dilates the anterior part of the nose, the valve region, in order to increase the air flow. Its inventors aimed to eliminate snoring and sleep apnoea using the device (Hoijer et al., 1992; Löth S and Petruson B, 1996; Petruson, B, 1990; Petruson B and Theman K, 1992). They have tested Nozovent in a number of studies and report an excellent effect on nasal resistance, snoring, and sleep apneas (Hoijer et al., 1992; Löth S and Petruson B, 1996; Petruson B, 1990; Petruson B and Theman K, 1992). However, Metes et al., (1992) did not find any effect on snoring, apnoeas, hypopnoeas, or arterial oxygen saturation (Sa,O_2) in a small sample of patients, despite a reduction in nasal resistance.

Nozovent is sold at pharmacies and is distributed worldwide as a treatment for different indications, such as compromised nasal breathing, nocturnal asthma, and dryness of mouth, snoring, and sleep apnoea. The potential market is huge, since habitual snoring occurs among 15% of middle-aged adults and occasional snoring among 30% (Gislason et al., 1988).

However, Bernd Schönhofer et al., (2000) did not recommend treatment with the Nozovent nasal dilator in patients suffering from OSAHS. The dilator has only a slight subjective effect on snoring, but no effect on objectively measured snoring and the other parameters of sleep-related breathing. Furthermore, when using a nasal dilator, it is possible that the bed partner's appreciation of the reduced snoring may delay the initiation of the adequate treatment of sleep apnoea.

Fig 2.13 Nozovent (nasal-valve dilator)



2.8.2 Surgical treatment

- **Tracheostomy**
- **Pharyngeal surgery (uvulo-palato-pharyngoplasty)**
- **Nasal surgery**
- **Maxillofacial surgery**
- **Adenoidectomy and tonsillectomy**
- **Tongue reduction**
- **Bariatric surgery**

In the treatment of OSAHS, surgical approaches have been proposed for identified levels of obstruction. Medical approaches are more commonly used; but not all patients are able or willing to conform to medical treatment. This group may be candidates for surgical intervention directed at the anatomical regions involved. During assessment of the patient, a surgical option can be considered, particularly in younger or middle-aged subjects, who may wish to avoid a period of attachment to CPAP or alternative medical devices.

Pre-surgical evaluation is important, in order to identify the type of anatomic abnormality present and the severity of the OSAHS. This will entail not only overnight polysomnography but also other investigations, such as cephalometric analysis, sleep nasendoscopy and three- dimensional MRI.

The American Sleep Disorders Association has produced recommendations for the use of surgical procedures in OSAHS. Desired treatment outcomes include resolution of the clinical signs and symptoms of OSAHS and normalisation of the apnoea / hypopnoea index and oxyhaemoglobin saturation levels. Because of the

complexity of airway narrowing or collapse during sleep, any one surgical procedure may not eradicate a patient's sleep apnoea. A stepwise approach to the surgical management would be acceptable if the patient is advised at the onset of treatment about the likelihood of the success of each procedure and that multiple operations may be necessary. Once the surgical site has healed, follow-up evaluation, including an objective measure of respiration and quality of sleep, must be performed to ensure that the abnormalities noted in the original study have been corrected.

2.8.2.1 Tracheostomy

Historically, the first surgical modality employed for the management of OSAHS was the tracheostomy, which proved effective in bypassing the impaired pharyngeal airway (Guyette RF and Waite PD, 1995).

Although improvement of the manifesting symptoms associated with the OSAHS condition is dramatic, patients may discover a whole new set of problems post operatively. These problems, which are associated with the surgical procedure, include bleeding, stoma, narrowing and granulation tissue formation.

Kim et al., (1998) undertook a retrospective study of all patients who had received a tracheostomy and who had been subjected to polysomnography since 1981 at the Johns Hopkins Sleep Disorder Centre. They concluded that tracheostomy effectively treated patients with 'uncomplicated' OSAHS but was considerably less effective in the treatment of patients with overlying cardiopulmonary decompensation.

Conway et al., (1981) published an article on the adverse effects of tracheostomy in which they highlighted the fact that a number of patients who had undergone

tracheostomy experienced tracheal granular malformation or stomal stenosis, necessitating revision procedures.

This, coupled with the considerable social disadvantage of the operation, means that tracheostomy for OSAHS is generally only used as a last resort, never as a treatment of first choice (Meyer et al., 1990).

The problems associated with the procedure have effectively relegated to the history books, however, in severe cases of OSAHS, which may be considered as life threatening, the tracheostomy may still be utilized as a final resort to treatment (Meyer JB and Knudson RC, 1990).

Postoperative wound infection and recurrent purulent bronchitis requiring hospitalization and / or antibiotics have been seen to occur, and reported psychological problems have included depression, substance abuse and marital problems (Conway et al., 1981).

Tracheostomy should only be considered when all else fails in carefully selected individual (SIGN, 2003).

2.8.2.2 Nasal surgery

The presence of nasal obstruction can both exacerbate the symptoms of OSAHS and inhibit optimal use of CPAP; common indications for nasal surgical reconstruction are:

- a) Septal deviation.
- b) Turbinate hypertrophy.
- c) Nasal polyps or chronic nasal congestion.

There is a considerable variety of opinion in the literature as to the efficacy of relieving nasal obstruction in OSAHS, with Olsen and Kern (1990) concluding

that relief of nasal obstruction does not resolve OSAHS whilst EL-Sharif and Hussein (1998) reported that 50% of 96 patients in their study obtained total relief, with a further 40% gaining some improvement.

Kuma and Sant' Amrragio (1991) recommended that intranasal procedures were useful in facilitating other non-surgical treatment regimens like nasal continuous positive airway pressure (nCPAP). This view is supported by Freidmann et al., (2000) who, in study of 50 consecutive patients with nasal airway obstruction and OSAHS, reported that although there was some improvement in nasal airway resistance, nasal surgery did not consistently improve the situation but may have contributed to a decrease in the required nCPAP pressure level and hence an improvement in oxygen saturation.

McDonald JP, (2003) in his review article concluded that intranasal surgical intervention is unpredictable in its effect on OSAHS.

The Scottish Intercollegiate Guidelines Network report (2003) on OSAHS recommended that alternative surgical approaches to OSAHS are experimental and should not be used outside the context of a randomised clinical trial (RCT).

2.8.2.3 Pharyngeal surgery (Uvulo-palato-pharyngoplasty)

The most widely used surgical treatment for Obstructive Sleep Apnoea / Hypopnoea Syndrome (OSAHS) and indeed snoring, is uvulo-palato-pharyngoplasty (UPPP), originally undertaken by surgical excision, more commonly now utilising a lazer (LAUP) (Kamami et al., 1994).

The original procedure was proposed by Ikematsu T, (1964), who reported on 152 patients with 82% relief from snoring. The technique was then introduced into the USA by Fijita et al., (1981) as an alternative to tracheostomy. The procedure was

initially devised to excise the uvula, the tonsils (if present), and portion of the soft palate, and to reorientate the tonsillar pillars in order to enlarge the oropharyngeal space, and therefore decrease pharyngeal collapsibility (Riley et al., 1987).

The rationale behind such procedure follows that if the soft palate is large and found to be the cause of pharyngeal obstruction, then its virtual removal would prove curative.

Fijita et al., (1981) suggested that anatomical indications for UPPP were a long uvula, redundant pharyngeal wall tissue, and / or excess tonsillar tissues.

Although subjectively it was thought to be curative procedure to many otorhinolaryngologists and their patients, the actual success rate for the procedure has been suggested to only 40.7% (Sher et. al., 1995).

Successful surgery was defined as a reduction in AHI to <10 or to <20 with a 50% reduction from the patients' baseline AHI.

A mandibular-hyoid distance (MP-H) $>20\text{mm}$ post-surgery was found to be significantly ($P=0.05$) predictive of failure of UPPP (Millman et al., 2000). The distance between the superior points of a line-constructed plane of the sphenoidale (Parallel to Frankfurt Horizontale) and a point at the intersection of the palatal plane perpendicular to the hyoid correlated negatively with post-surgical AHI. An MP-H distance of $<21\text{mm}$, an angle created by point 'A' to Nasion to point 'B' <3 , and the presence of baseline AHI >38 enhanced the predictability of UPPP success (Millman et al., 2000).

Walker-Engstrom et al., (2000) studied ninety-five patients with mild to moderate obstructive sleep apnoea / hypopnoea syndrome (Apnoea Hypopnoea Index AHI >5). These patients were randomly allocated to either a dental appliance or UPPP treatment group. Seven patients withdrew after randomisation but before

treatment, leaving 88 patients eligible for the study. The patients were examined using somnography and administered the Minor Symptoms Evaluation-Profile (MSE-P), a QOL questionnaire, before and 1 year after intervention. Thirty-seven patients in the dental appliance group and 43 in the UPPP group completed the 1-year follow-up. The mean values for the three dimensions vitality, contentment and sleep improved significantly 1 year after intervention in the dental appliance and UPPP groups. No difference in the QOL scores at baseline was noted between the groups. One year after intervention, the UPPP group showed significantly more contentment than the dental appliance group. In contrast, vitality and sleep dimensions did not differ between the two treatment groups. No significant correlations were observed between the QOL scores and somnographic values. In conclusion, quality of life improved significantly in the dental appliance and UPPP groups 1 year after intervention. However, the dental appliance group showed a lower level of contentment than the UPPP group possibly due to the continuation of the dental appliance, even though the somnographic values were superior in the former group.

A recent meta - analysis review of LAUP suggested that the procedure should not be used for the treatment of patients with any significant OSAHS (Verse et al., 2000). Battagel et al., (1996) supported minimalist LAUP for those patients who snore loudly with no symptoms of OSAHS.

It is important to differentiate, when using UPPP or related surgical operations, between those patients who are 'simple snorers' and those who exhibit clinical OSAHS. The operation is widely used on the former group and it is suggested that a sleep study assessment to exclude OSAHS is undertaken, given that there is considerable evidence that UPPP has an adverse effect on the patient's subsequent

ability to use nCPAP, should they subsequently develop OSAHS (Mortimer et al., 1996; Janson et al., 2000).

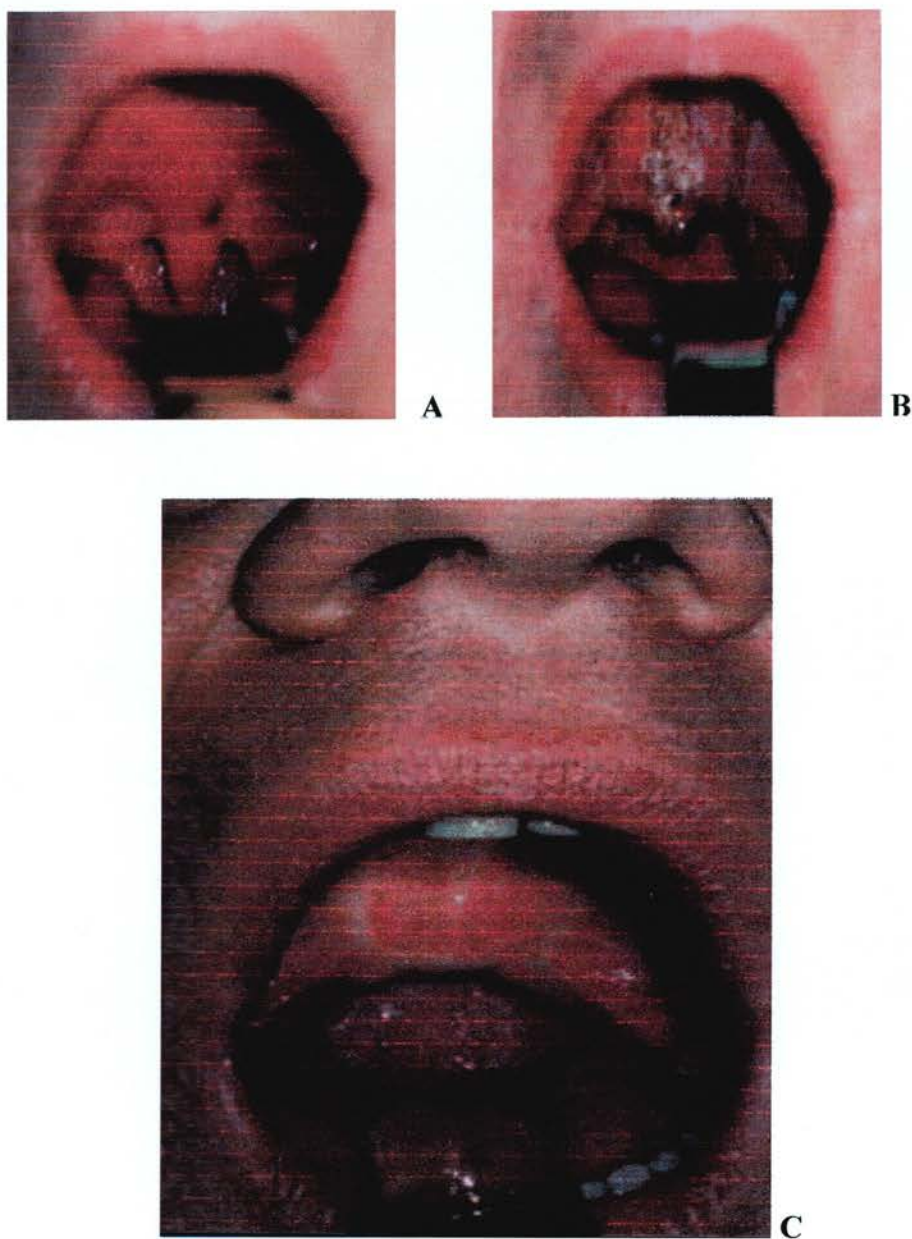
However, the operation is not without side effects. Apart from significant pain, immediate post - operative inability to seal the nasal from the oral cavity is common. Long-term fistulae, palatal stenosis, and alterations in voice have also been reported (Riley et al., 1987 and 1990a).

More-over, the operation is not always successful (Riley et al., 1987 and 1990b) as any obstruction may be present at more than one site or occur lower down in the airway, thus will be unaffected by (UPPP).

Where the subjects are loud snorers, however, this symptom usually improves. For this reason, palatal surgery, now offered as a minimal laser procedure, may be of benefit to subjects who snore, but only after a diagnosis of OSAHS has been excluded (MacDougland 1994; Battagel et al., 1996).

Fig 2.14

Uvulo-palato-pharyngoplasty



Uvulo-palato-pharyngoplasty (Laserbatten)

- A. Pre-operative photo shows an enlarged soft palate and midline uvula can be noted.
- B. Post-operative photo shows shortened soft palate together with the Laser created 'battens' in the soft palate.
- C. Three month after surgery shows the healed soft palate with the three battens visible as white lines within the soft palate.

Taken from www.snoring.com.au

2.8.2.4 Maxillo-facial surgery

- *Geniotubercle advancement*
- *Hyoid suspension*
- *Advancement genioplasty*
- *Mandibular advancement*
- *Bimaxillary advancement*

Mandibular retrognathia has been linked with OSAHS. The link is explained by the resulting repositioning of the tongue and consequential obstruction of the pharyngeal space. During the 1980's, the recognition of the importance of the tongue position led to the application of orthognathic surgical procedures for the management of OSAHS. The procedures involved may range from simple geniotubercle advancement to the more complex bimaxillary advancement with or without genioplasty and the hyoid suspension. The report of maxillofacial surgery appears good, with 97% control of sleep apnoea despite some surgical mandibular relapse (Riley et al., 1987 and 1990a).

2.8.2.4.1 Geniotubercle advancement

The geniotubercle advancement or 'geniotomy' as it is sometimes known was a surgical approach developed by Riley et al., (1987). The procedure is designed to advance the tongue without having any significant effects upon lower facial aesthetics, and is particularly useful in cases where mandibular dimensions are 'normal'. The surgery involves sectioning a central block of bone beneath the lower incisors (including the genial tubercle), and advancing the segment

anteriorly. As a consequence of the advancement of the attachments for the genioglossus and the geniohyoid muscles both the tongue and the hyoid bone are likewise advanced.

2.8.2.4.2 Hyoid suspension

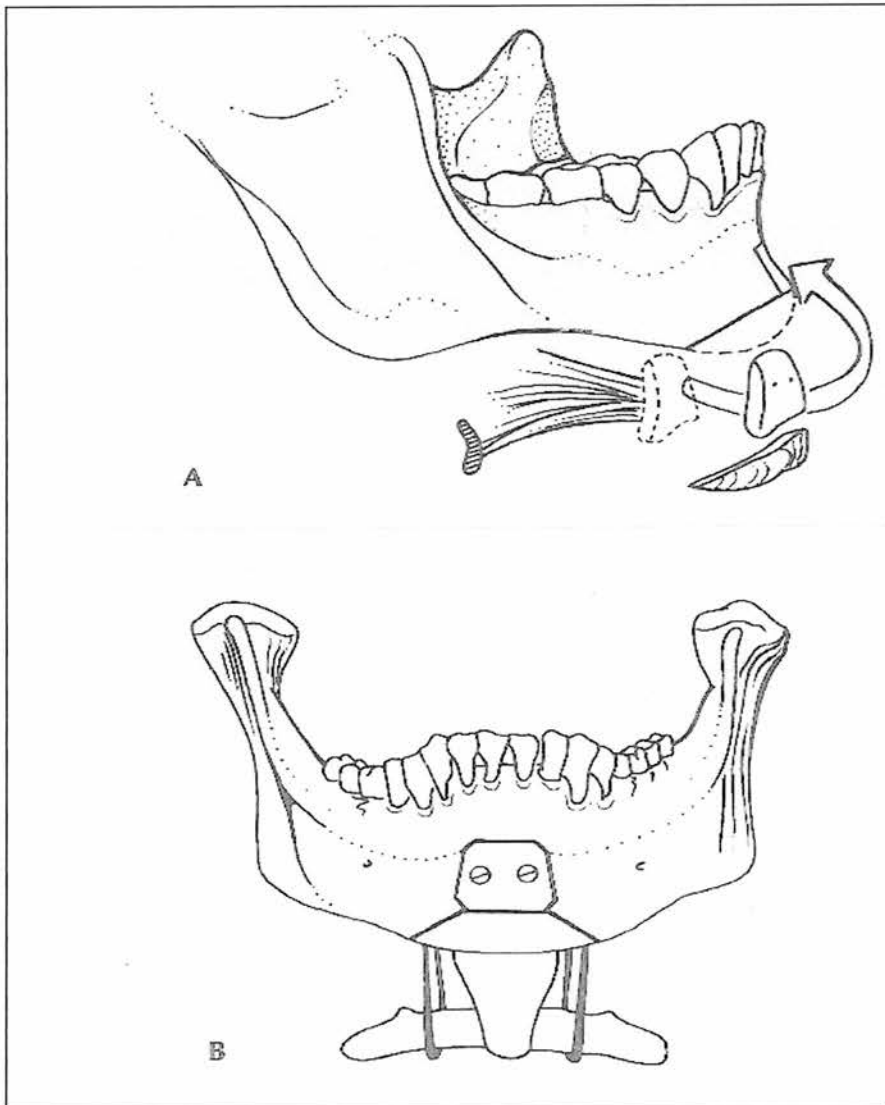
Adjunctive procedures such as hyoid suspension using facial lata harvested from the thigh are sometimes employed to advance the hyoid bone, opening up the hypopharyngeal region via its attachments to the epiglottis, vallecula and tongue base. Unfortunately, hyoid suspension as an isolated procedure has failed to demonstrate any real benefit and is therefore often undertaken only in conjunction with geniotubercle advancement (Riley et al., 1990a).

2.8.2.4.3 Advancement genioplasty

When the chin is deficient, a standard advancement genioplasty has proven to be quite useful in the treatment of OSAHS. Besides the obvious aesthetic advantages, the procedure also brings forward anterior digastric muscle attachments, effectively providing forward traction to the hyoid bone and consequential tendency to open up the hypopharynx.

Fig 2.15

**Genioglossal advancement with hyoid
myotomy and suspension**



- A. Diagrammatic representation of the anterior movement of the freed segment of mandible with the attached genioglossus to its new position anterior to the mandible.
- B. The freed segment of mandible is fixed in position anterior to the mandible. The hyoid is freed from its inferior attachments in the neck and suspended from the anterior mandible by strips of fascia lata.

(Taken from Sher AE et al., The Efficacy of surgical modifications of the upper airway in adults with OSAHS. *Sleep* 1996; 19: 156-177).

2.8.2.4.4 Mandibular advancement

In those cases with a cephalometrically measured retrognathic mandible, it is possible to use a mandibular repositioning appliance as a diagnostic aid, in order to establish the efficacy of moving the mandible forward before undertaking actual surgery (McDonald JP, 2003).

Riley R and Powell NB (1990) found that 65% of patients under their care improved with mandibular forward osteotomy surgery. Lowe AA, (1993) agreed that the procedure was beneficial but only where the obstruction was in the hypopharynx. Yu et al., (1994), however, found mandibular advancement to be an unpredictable procedure.

The only disadvantage to this approach, is the prolonged period of pre-surgical orthodontic treatment often necessary to decompensate the dental arches so that a functional long - term occlusion may be attained.

2.8.2.4.5 Bimaxillary advancement

Although traditionally bimaxillary advancement surgery was originally reserved only for those OSAHS subjects with 'major' skeletal base discrepancy, the simultaneous advancement of the maxilla (Le Fort I down fracture osteotomy), and of the mandible (bilateral sagittal split osteotomy), is becoming more popular approach for OSAHS subjects who have failed to accommodate or respond to other more conservative treatment modalities. In fact, Riley et al., (1990a) have demonstrated that the bimaxillary advancement procedure is the most successful surgical procedure so far developed for the management of OSAHS. They reported good success rate, with 97% control of the sleep apnoea despite some postoperative surgical mandibular relapse. Furthermore, advancement genioplasty

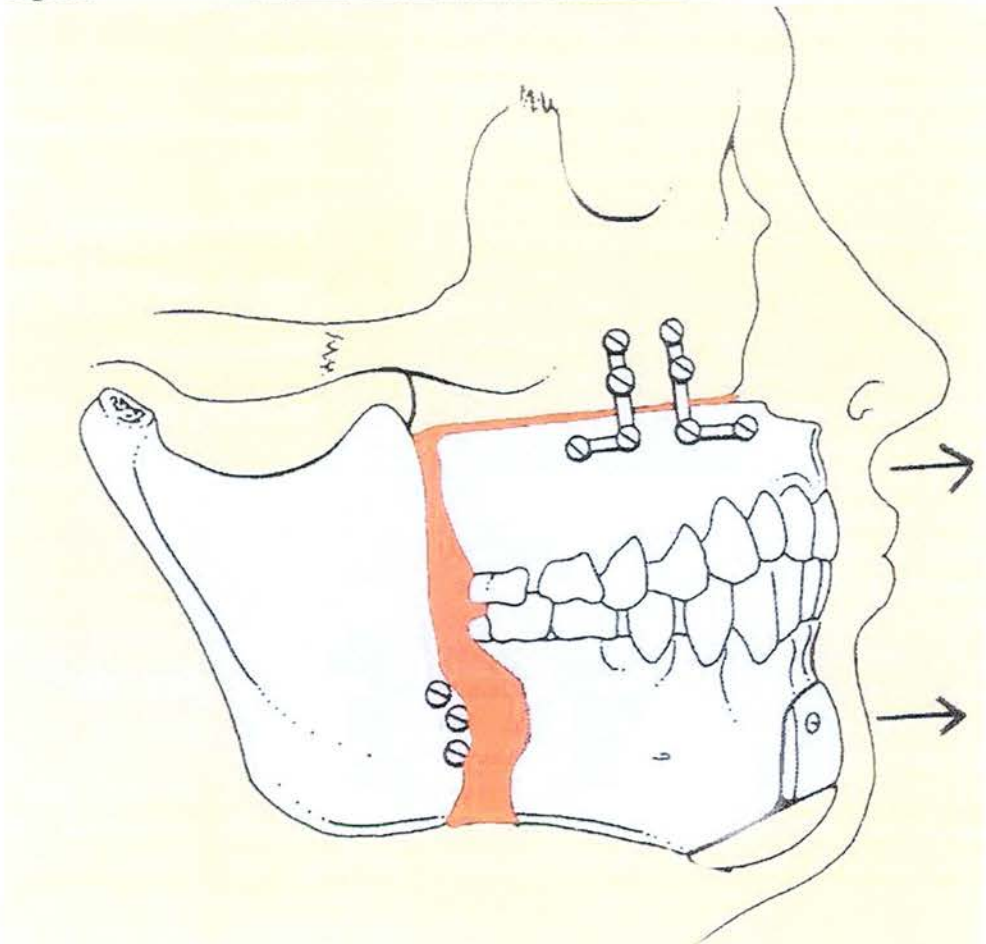
or geniotubercle advancement may also further augment the pharyngeal space when undertaken together with the bimaxillary advancement surgery. Where both jaws are advanced by the same amount, no pre-surgical orthodontic procedures are normally required. Waite PD (1998) and Krekmanov et al., (1998) suggested that the maxillary / mandibular advancement using Le Fort I and surgical splint mandibular osteotomies, permitted greater forward movement of the mandible whilst preserving the occlusion. Postoperative success has proved to be stable over a two-year period (Conradt et al., 1997).

In cases where unequal jaw surgery advancement is necessary, orthodontic is essential to prepare the occlusion prior to surgery, to ensure that profile changes are minimised and that the post surgical occlusion is acceptable (Battagel et al., 1996).

On the evidence available, therefore, maxillary / mandibular advancement remains largely untested (McDonald JP, 2003).

Fig 2.16

Maxillo-mandibular advancement



Taken from McDonal JP (2003), the Surgeons: 5: 259-264

2.8.2.5 Tonsillectomy and adenoidectomy

OSAHS may also be diagnosed in children, which may frequently be associated with tonsillar and adenoid hypertrophy. Such patients are recommended by Linder-Aronson (1979), for tonsillectomy and / or adenoidectomy procedures to 'cure' sleep apnoea, snoring, daytime sleepiness, mouth breathing and abnormal facial growth. Affected children tend to be shorter in stature than their peers (Battagel et al., 1996). It has been suggested that hypertrophic tonsils alone does not give rise to OSAHS (Battagel et al., 1996).

2.8.2.6 Tongue reduction

Djupesland et al., (1992); Midjejeig H and Trinnereim M, (1992) described an operation termed uvulo-palato-pharyngo-glossoplasty (UPPGP) which incorporated a modified UPPP with limited resection of the tongue base. Fujita et al., (1990 and 1991) and Woodson et al., (1992) under took midline glossectomy and ligualplast to create an enlarged retrolingual airway.

Chabolle et al., (1991) combined tongue base reduction with hyo-epiglossoplasty in a small study of 10 patients and reported considerable improvement.

Tongue reduction procedures have not been popular because of its complications. Most are done only after a tracheostomy is undertaken due to the associated oedema. Tongue reduction surgery is reserved for unusual cases of OSAHS, such as acromegally or marked macroglossia as in trisomy-21 children.

2.8.2.7 Bariatric surgery

Weight loss is an effective treatment for OSAHS, so it would follow that bariatric surgery would be efficacious (Harman et al., 1982; Smith et al., 1985; Surat et al.,

1986). Meyer et al., (1996) noted the relationship between BMI, age and upper airway measurements in snorers and sleep apnoea patients.

Charuzi et al., (1992) reported on a case series of 47 morbidly obese subjects followed-up after one year and again after seven years following surgery. They reported a significant decrease in the number of apnoeic episodes per hour of sleep, due primarily to the weight loss. It was noted that those individuals who subsequently gained weight began to increase the frequency of apnoeic episodes.

Sugarman et al., (1992) reported on 126 patients treated by bariatric surgery over a 10-year-period. Of the 40 patients with pre- and post- weight reduction sleep polysomnograms, the sleep apnoea index fell from 64 ± 39 to 26 ± 26 ($P < 0.0001$), and was associated with significant improvement in other measurable sleep indices.

Dhabuwala et al., (2000) noted an improvement in co-morbidly factors following weight loss from gastric bypass surgery.

There is, however, as yet no controlled trial available on the efficacy of bariatric surgery in inducing weight loss and improvement in clinical outcome (McDonald JP, 2003).

Table 2.3

Key features in the treatment of OSAHS

1. All patients with suspected sleep apnoea / hypopnoea syndrome and their partners should complete an Epworth questionnaire to assess the degree of pre-treatment sleepiness (Johns et al., 1991). If OSAHS is suspected, then polysomnography should be undertaken to confirm the diagnosis.
2. Weight loss without resort to bariatric surgery should be encouraged where it is contributing to OSAHS.
3. CPAP therapy is the first choice therapy for moderate to severe patients; intra-oral devices are an appropriate therapy for snorers and mild OSAHS sufferers.
4. Use of UPPP or LAUP for the treatment of OSAHS, as opposed to simple snoring is not recommended.
5. Palatal surgery can compromise later CPAP use if the patient later develops OSAHS.

Taken from McDonal JP (2003), *the Surgeons*: 5: 259-264

Surgical complications

Despite the apparent success rates of some surgical technique used to manage OSAHS, there are also significant drawbacks. These include both intraoperative and immediate postoperative complications such as haemorrhage, infection, airway obstruction and anaesthetic complications. Other suggested problems include the distortion of the abnormal loading of the temporomandibular joints, prolonged intermaxillary fixation, a negative aesthetic impact, temporary or indeed permanent anaesthesia, instability of the skeletal advancement and perhaps most importantly, the inability to provide an accurate long-term prognosis due to a lack of adequate data. It must be stressed that OSAHS patients frequently present with other medical problems, which unlike routine orthognathic cases, may necessitate careful preoperative medical assessment and treatment and of course special anaesthetic care.

AIMS OF THE STUDY

The aim of this study was to perform a systemic and detailed cephalometric analysis in a group of adult patients diagnosed with OSAHS, and to compare this with the data obtained in a control group consisting of healthy individuals without the cardinal symptoms of OSAHS.

To determine if there are significant differences in craniofacial morphology and the position of the hyoid bone in relation to the cervical vertebrae and / or a fixed point upon the anterior cranial base.

To suggest possible skeletal morphology for the OSAHS patients.

Accordingly the aims of this investigation are: to investigate the following ‘null hypotheses’:-

1. The craniofacial morphology and the position of the hyoid bone in relation to the cervical vertebrae and / or a fixed point upon the anterior cranial base, provides no indication as to the severity of OSAHS.
2. There are no significant differences in skeletal morphology between the OSAHS group and the controls matched for sex, age and the ethnicity.

MATERIALS

- 4.1 The subjects.**
- 4.2 The control group.**
- 4.3 Cephalogram.**
- 4.4 Lateral cephalometric films.**
- 4.5 Computer and software.**
- 4.6 X-ray viewer (light box).**
- 4.7 Accessories.**

The material for this study comprised the anomaly group, control group, cephalogram, lateral cephalometric films, computer and software, x-ray viewer, and the accessories. The sample of the anomaly and the control were not restricted in any way by malocclusion but it was decided that due to the nature of the variables chosen, subjects would all be dentate. This was to maintain standard cephalometric tracing in all subjects.

4.1 The Subjects

The subjects selections were based on the following:-

- All subjects were previously diagnosed with OSAHS by polysomnographic diagnostic sleep studies (Edinburgh Sleep Laboratory) before presenting to the orthodontic clinic.
- The group consisted of 65 white Caucasian adults' (50 males, 15 females), and their age ranged between 25-75 years.
- Subjects had not undergone any surgery for the treatment of OSAHS.

4.2 The Control Group

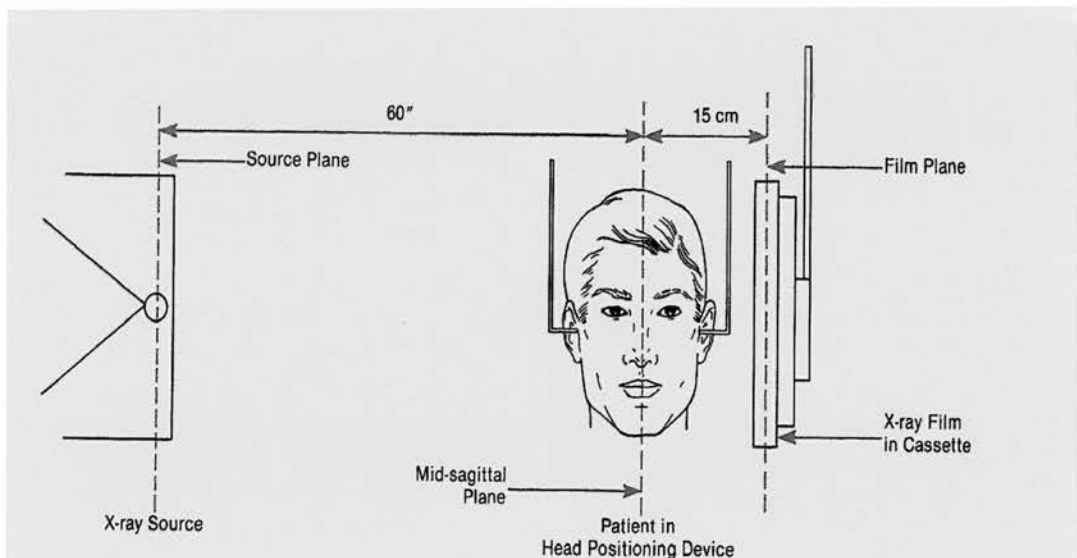
The control group selections were based on the following:-

- All subjects were asked if they had ever been known to snore. This was verified whenever possible by a sleeping partner.
- The group consisted of 30 white Caucasian adults' (23males, 7 females) between 25-55 years, matched for sex and ethnicity to the subjects.
- All subjects were in good medical health and did not suffer from any airway disease.

4.3 Cephalogram

All the lateral cephalogramic radiographs were taken using a Siemens Orthophos CD at the Royal Infirmary of Edinburgh Radiography Department which has a cephalostat with identifying screen and motorizes adjustable grid. The KVP (peak kilovoltage) was adjusted to optimize the contrast of both hard and soft tissues. The distance from the focus to the median plane was 60 inches, (152 cm) and the median plane to the film was 15 cm, (Proffit, 2000).

Fig 4.1 **The cephalogram**



Diagrammatic Representation of The Standard Cephalometric Arrangement

By convention, the distance from the x-ray source to the subject's midsagittal plane is 5 feet, and the distance from the midsagittal plane to the cassette is fixed for 1 foot for all patients.

Taken from 'Contemporary Orthodontics', Proffit 2000

4.4 Lateral cephalometric films

The lateral cephalometric films used in this study were Konica, 18 × 24 cm, Konica Europe GmbH, Friedrich-Bergius-Str., Gewerbegebiet, 85662 Honenbrunn, Germany. The films were stored in a cool, dry place and adequately protected from x-rays, Gamma rays and others. The internal film package was retained for additional light protection.

Fig 4.2 The x-ray film



4.5 Computer and software

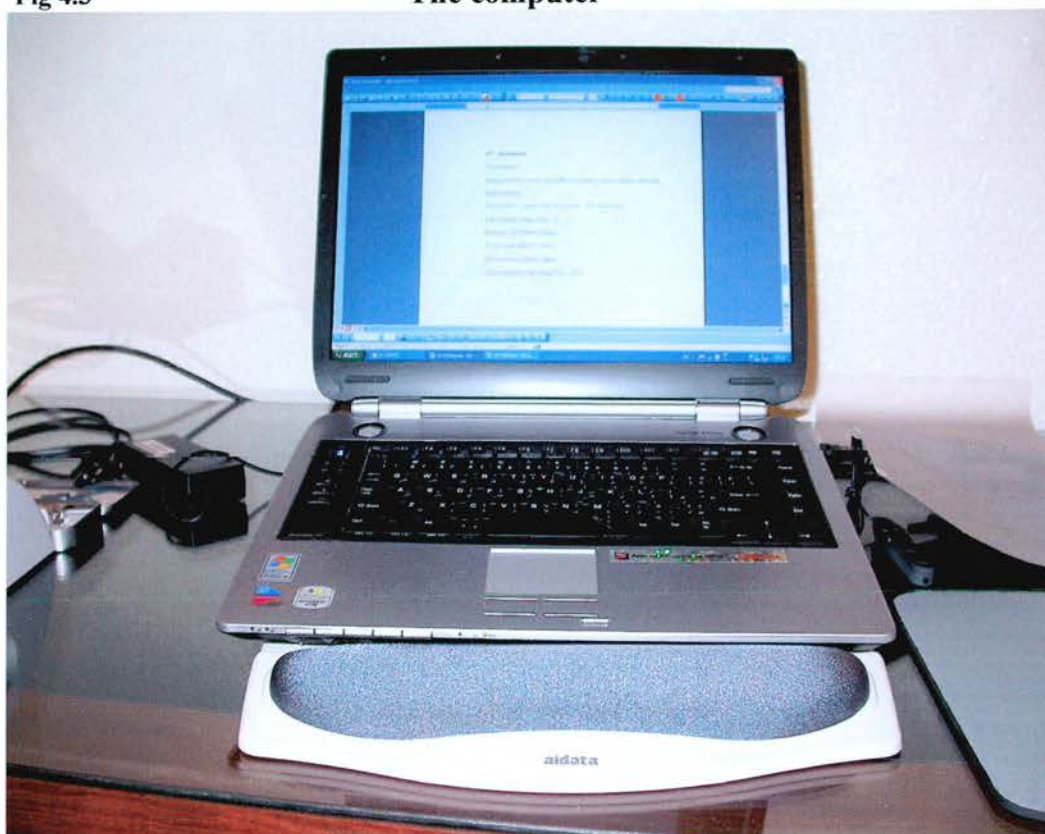
Toshiba portable computer was used with Centrino™ mobile technology.

Microsoft® windows® XP with Microsoft Office 2003 software.

Statistical software: SPSS for windows version 10.0 (Norusis MJ), [Prentice-Hall Inc., A Simon & Schuster Company, Upper Saddle Drive, New Jersey, USA].

Fig 4.3

The computer



4.6 X-ray viewer

Model: light box, from RMO[®] by Numonics Corporation, 101 Commerce Drive, Montgomeryville, Pa 18936, USA.

Serial no: 047776

Voltage: 220 V

Hz: 50 – 60

Amperes: 1A

Fig 4.4

The x-ray viewer



4.7 Accessories

Tracing papers

Pencils (Staedtler, Noris 122, made in Germany), easy to sharpen with high break resistance.

Eraser (Faber – Castell, made in Germany), 7092 vinyl eraser.

Ruler (Crystal, India), 20cm - 8".

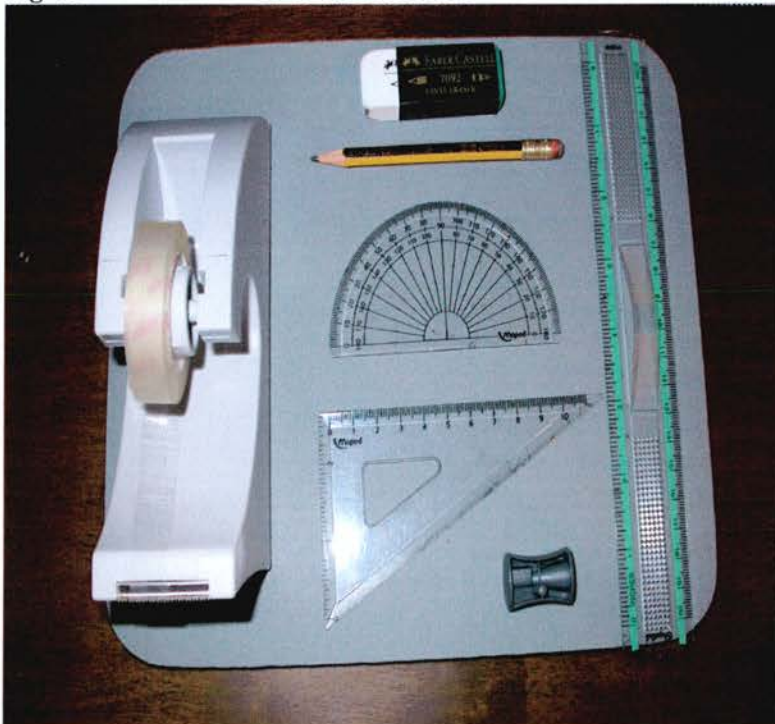
Protractor 180° (Maped, China).

60° set square (Maped, China).

Pencil sharpener (Maped, China).

Celluloid adhesive tape (Eagle[®] TY – 895).

Fig 4.5 **The accessories**



METHODOLOGY

5.1 Subjects and controls selection

5.2 Lateral cephalometric radiograph

5.3 Cephalometric analysis

5.4 Method error

- **Random error**
- **Systemic error**
- **Calculation error**

5.5 Data analysis

5.1 Subjects and control selection

The records of sixty five white Caucasian adult subjects (50 males, 15 females), aged between 25 to 75 years, who had undergone polysomnographic testing at the Edinburgh Royal Infirmary Sleep Clinic and subsequently were found to have OSAHS, were randomly selected for assessment. All patients had a history of disturbed sleep, characterized by heavy snoring and recurrent apnoeic periods, as well as excessive day time sleepiness. They underwent a physical evaluation, including head and neck and neurological examination, pulmonary and cardiac function tests and 24-hour Halter ECG (Tilkian, 1977).

The AHI range for the subject group was between (10 and 206 per night), with a mean value of 16.4 per hour, and a distribution approximating that of the population examined within the sleep clinic; i.e. a greater number of subjects displaying relatively lower AHI values as compared with extreme values of 40 and above.

Those subjects who were subsequently referred to the Victoria Hospital (Kirkcaldy, Fife, Scotland) for treatment with Mandibular Repositioning Appliance were 'marked' and are presumed to represent the portion of the investigated population deemed to suffer from a mild to moderate form of Obstructive Sleep Apnoea / Hypopnoea Syndrome (OSAHS).

All-night polysomnographic recording documented the presence of OSAHS in all subjects. The sleep recording included electroencephalogram (EEG), electrocardiogram (ECG), electrooculogram (EOG), electromyogram (EMG), thoracic respiratory movements, oro-nasal flow, and oxygen saturation using pulse oximetry (Rechtschaffen A and Kales A, 1968).

The control group consisted of thirty (30) healthy white Caucasian adults (23 males, 7 females), free from OSAHS symptoms, selected from patients visiting different dental clinics at Edinburgh Postgraduate Dental Institute in November 2001. Their ages ranged between 25-55 years. The demographic data are summarized in Table 5.1.

Table 5.1 Demographic data for the OSAHS subjects and the control

	OSAHS group (n=65)		Control group (n=30)	
	Mean	Range	Mean	Range
Age (years)	47.5	25-75	42.8	25-55
BMI (kg/m²)	28.7	23.8-44.1	24.2	21.7-26.9
PPNC (%)	101.5	95.9-121.4	95.7	83.1-110.2

5.2 Lateral Cephalometric Radiograph

All the lateral cephalograms were taken using a Siemens Orthophos CD at the Royal Infirmary of Edinburgh Radiography Department which has a cephalostat with intensifying screen and motorizes adjustable grid. The KVP (peak kilovoltage) was adjusted to optimise the contrast of both hard and soft tissues. The distance from the focus to the median plane was (60 inches, 152cm) and the median plane to the film was (15cm) (Proffit, 2000). The subject was standing upright with ‘natural’ head position that is the ‘natural’ posture of the head when standing with the visual axis being horizontal (Broca, 1862). Such a standardized position has been investigated by Solow and Tallgren (1971), who provided a

detailed description of the method. Initially the subject assumes the “orthoposition” defined by Molhave (1958) as the ‘intention’ position from standing to walking. The median plane parallel to the film with the maximal intercuspatation of the teeth and lips in light contact, and in natural head position (Moorees and Kean, 1958). A possible lateral head tilt or rotation was prevented by means of a cross-light beam projected onto the face and finally, the bilateral ear rods were gently inserted onto the external part of the auditory meatus to stabilize the head posture during exposure. All lateral cephalograms were taken before any medical or surgical intervention.

Radiographs were traced, oriented with the maxillary plane horizontal and skeletal points identified (Fig. 5.2). Definitions of the landmarks are given in the accompanying legend. Points were digitized twice (one week interval) in a predetermined sequence to a tolerance of 0.2 mm and the mean value taken.

The reference points and lines used in this research are given in Figs (5.3, 5.4, 5.5, 5.6, 5.7 and 5.8). The definitions are taken from Solow, 1966; Solow and Greve, 1979; Lyberg et al., 1989. Some unfamiliar landmarks, planes and measurements which are not described in these papers are described and explained in details.

Fig 5.1

Lateral cephalometric radiograph



5.3 Cephalometric Analysis

Radiographs were traced to allow identification of specific points and planes, which in turn allowed appropriate measurements to be made. Tracing was performed in a darkened room on a well-illuminated viewing screen / tracing box using good quality acetate tracing paper and a 4H pencil. Eleven hard tissue points were identified (Table 5.2) which allowed the plotting of the six reference planes necessary for the measurements required, (Table 5.3 and figure 5.4).

All measurements were adjusted for magnification factor, which could be measured directly from radiographs through the inclusion of a perpendicular ruler (Figure 5.2). This was found to be consistent at 10%.

Fig 5.2

Cephalometric Landmarks

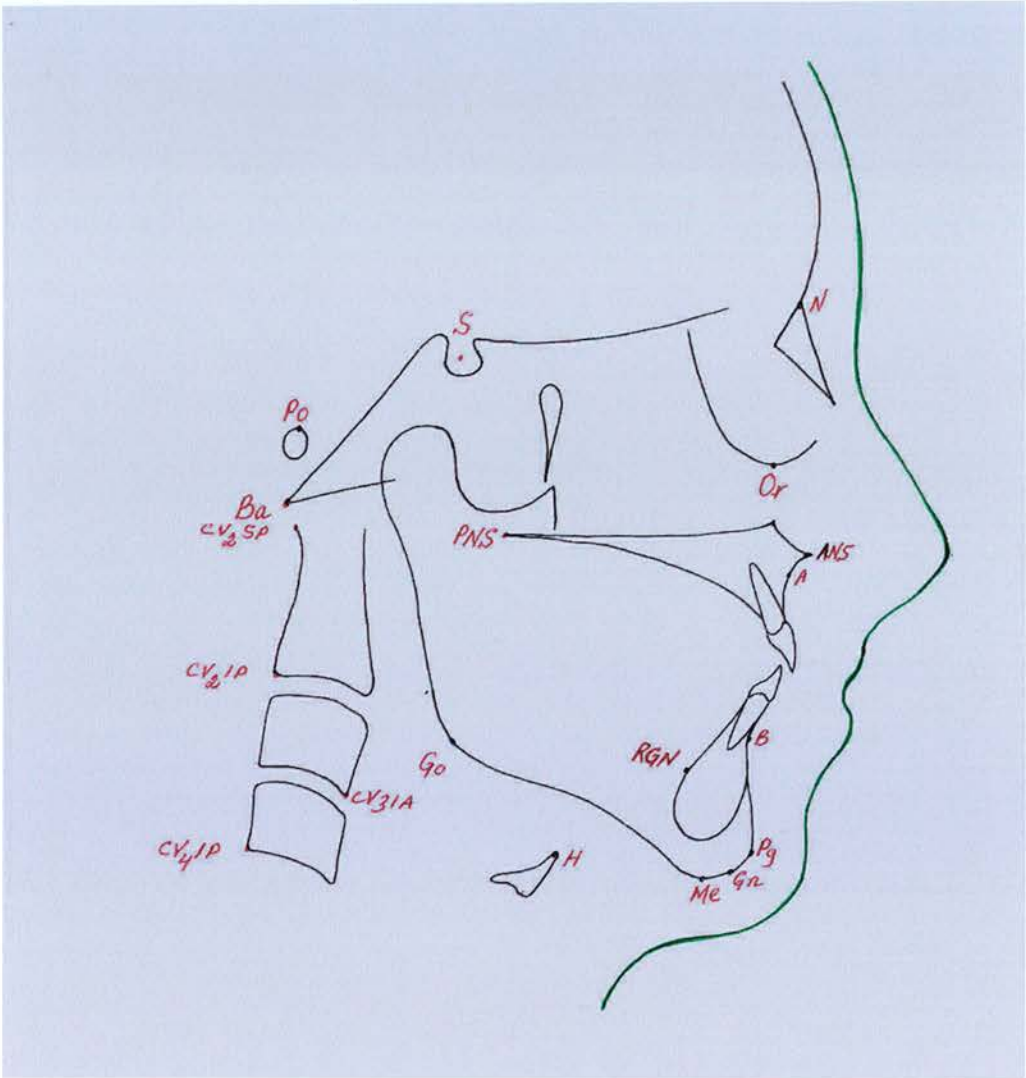


Table 5.2

Anatomic landmarks

Points	Description
N	Nasion. The most anterior point of the frontonasal suture.
S	Sella. The midpoint of the sella tursica.
Or	Orbitale. The deepest point on the infra-orbital margin.
Po	Porion. The uppermost, outermost point on the bony external auditory meatus
ANS	Anterior Nasal Spine. The tip of the anterior nasal spine.
PNS	Posterior Nasal Spine. The tip of the posterior nasal spine.
A	Subspinale. The most posterior point on the anterior contour of the upper alveolar process.
B	Supramentale. The most posterior point on the anterior contour of the lower alveolar border.
Me	Menton. The lower most point on the mandibular symphysis in the midline
Gn	Gnathion. The most inferior point on the mandibular symphysis.
Pg	Pogonion. The most anterior point on the mandibular symphysis.
RGN	Retrognathion. The most posterior point of the mandibular symphysis along a line perpendicular to the FH (Frankfurt Horizontal) plane.
cv2sp	The most posterior-superior point on the corpus of the 2 nd cervical vertebra.
cv2ip	The most inferior-posterior point on the corpus of the 2 nd cervical vertebra.
cv3ia	The most inferior-anterior point on the corpus of the 3 rd cervical vertebra.
cv4ip	The most inferior-posterior point on the corpus of the 4 th cervical vertebra.

Fig 5.3

Reference lines

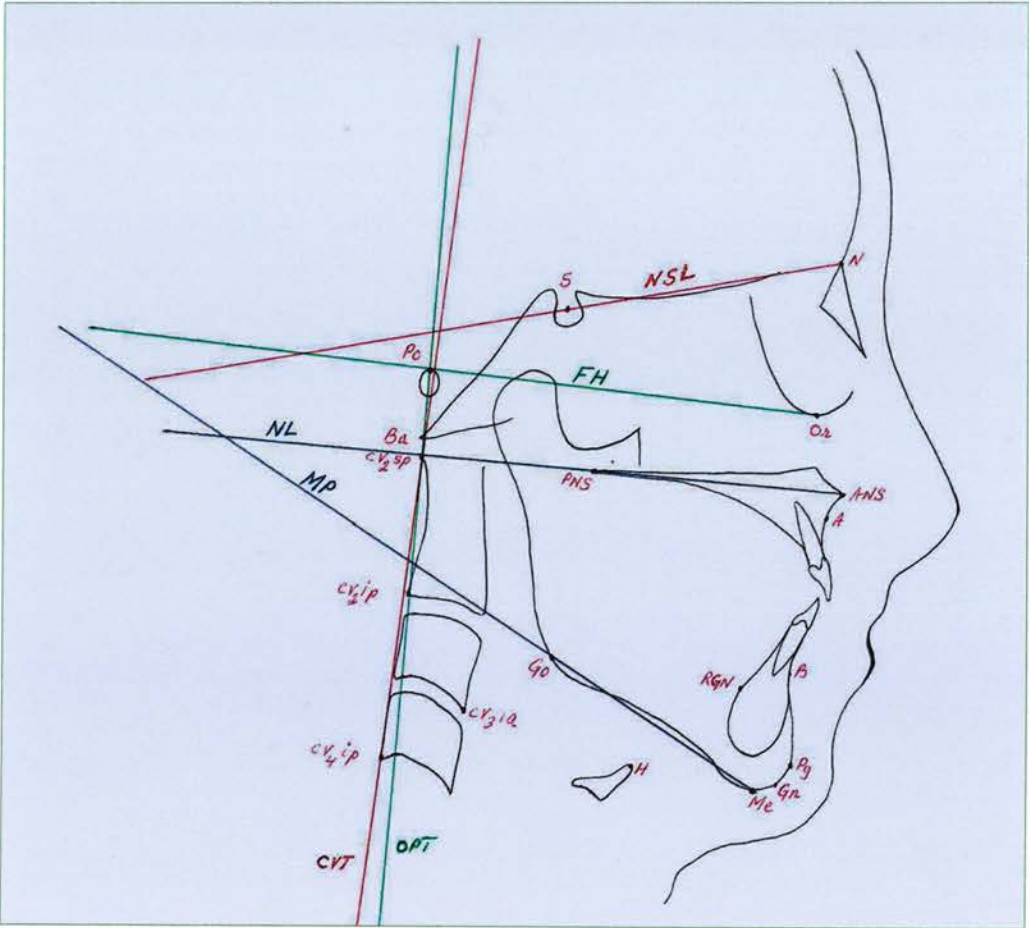


Table 5.3

Reference lines definition

Lines / Planes (mm)	Definition
NSL	Nasion - Sella Line. The line through points N and S.
FH	Frankfurt Horizontal. The line through point Or and Po.
NL	Nasal Line (Maxillary Plane). The line connecting ANS with PNS.
MP	Mandibular Plane. The line to the lower border of the mandible joining Me and Go.
CVT	Cervical Vertebra Tangent, which passes through cv2sp and cv4ip.
OPT	Odontoid Process Tangent, which passes through cv2sp and cv2ip.

Figure 5.4 **Angular measurements**
(Natural head postures and cranio-cervical variables)

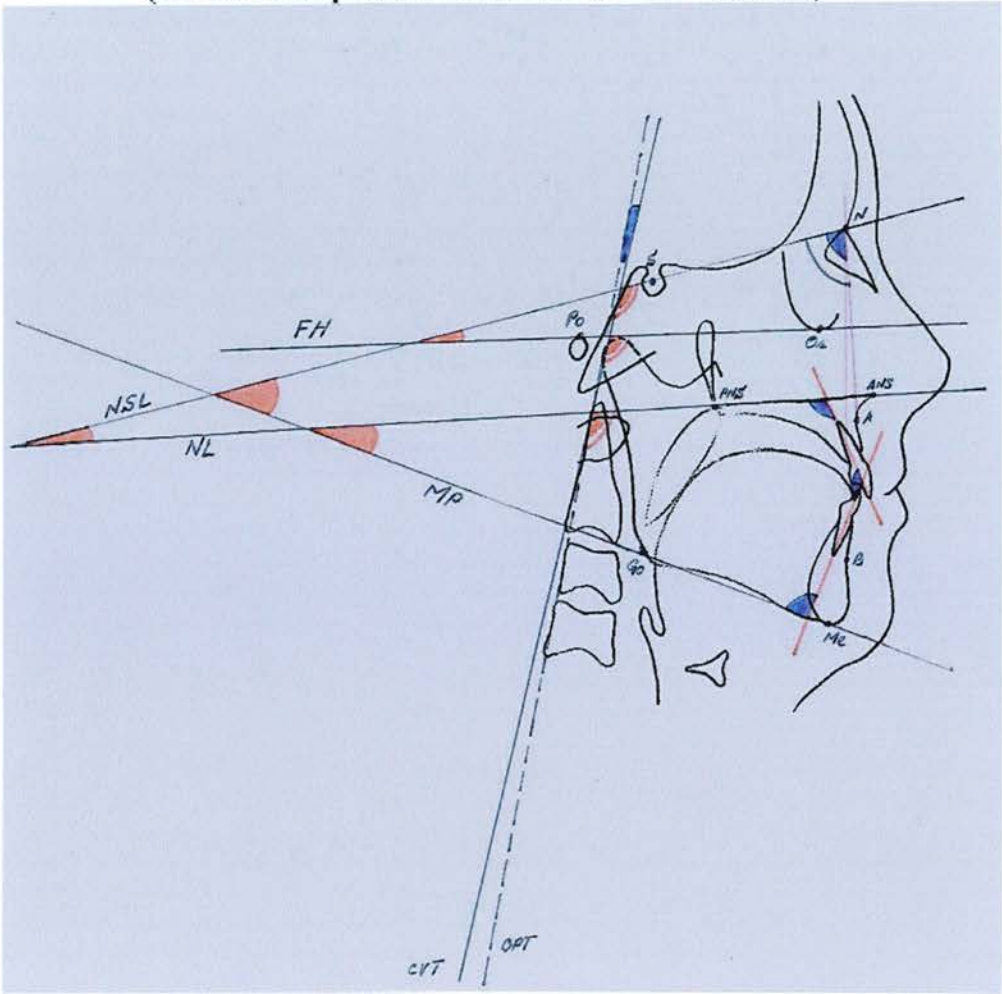


Table 5.4 Angular measurements (Natural head postures variables)

Variables	Description
NSL/OPT	The angle between the Sella-Nasion line and the Odontoid process tangent.
FH/OPT	The angle between Frankfort horizontal and the Odontoid process tangent.
NL/OPT	The angle between the nasal line and the Odontoid process tangent.
NSL/CVT	The angle between the Sella-Nasion line and the cervical vertebra tangent.
FH/CVT	The angle between Frankfort horizontal and the cervical vertebra tangent.
NL/CVT	The angle between the nasal line and the cervical vertebra tangent.
OPT/CVT	The angle between the Odontoid process tangent and the cervical vertebra tangent.
NL/NSL	The angle between the nasal line and Sella-Nasion line.
MP/NSL	The angle between the mandibular plane the Sella-Nasion line.
NL/MP	The maxillary mandibular plane angle.
FH/NSL	The angle between Frankfurt horizontal and Sella-Nasion line.

Table 5.5 Angular measurements (Craniofacial variables definition)

Variables	Description
SNA	Anteroposterior position of the maxilla.
SNB	Antero-posterior position of the mandible.
ANB	The difference between SNA and SNB.
U1/L1	The angle between the long axis of the upper and lower incisors.
U1/NL	The long axis of the upper incisor to the maxillary (nasal) plane, (Maxillary incisor inclination).
L1/MP	The long axis of the lower incisor to Mandibular plane, (Mandibular incisor inclination).

Fig 5.4 Linear measurements (Craniofacial variables)

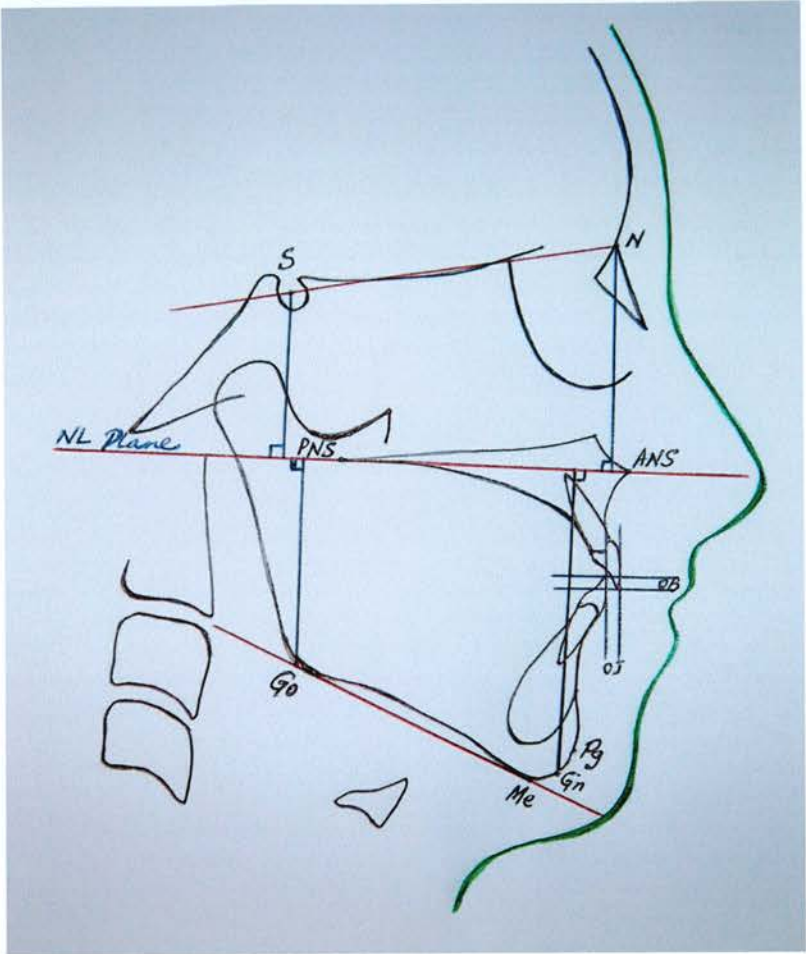


Table 5.6 Linear measurements (Craniofacial variables definition)

Variables	Description
N–NL	Upper anterior face height. The perpendicular distance from point N to NL.
Gn–NL	Lower anterior face height. The perpendicular distance from point Gn to NL.
S–NL	Upper posterior face height. The perpendicular distance from point S to NL.
Go–NL	Lower posterior face height. The perpendicular distance from point Go to NL.
N–S	NSL, (Nasion-Sella Line). Anterior cranial base length.
ANS–PNS	Maxillary length. The tangent connecting ANS with PNS.
Me–Go	Mandibular length. The tangent connecting Go to Me.
Overbite	The overlapping of the lower incisors by the upper incisors.
Overjet	The horizontal distance between the upper and lower incisors.

Fig 5.5 Linear measurement (Hyoid bone variables)

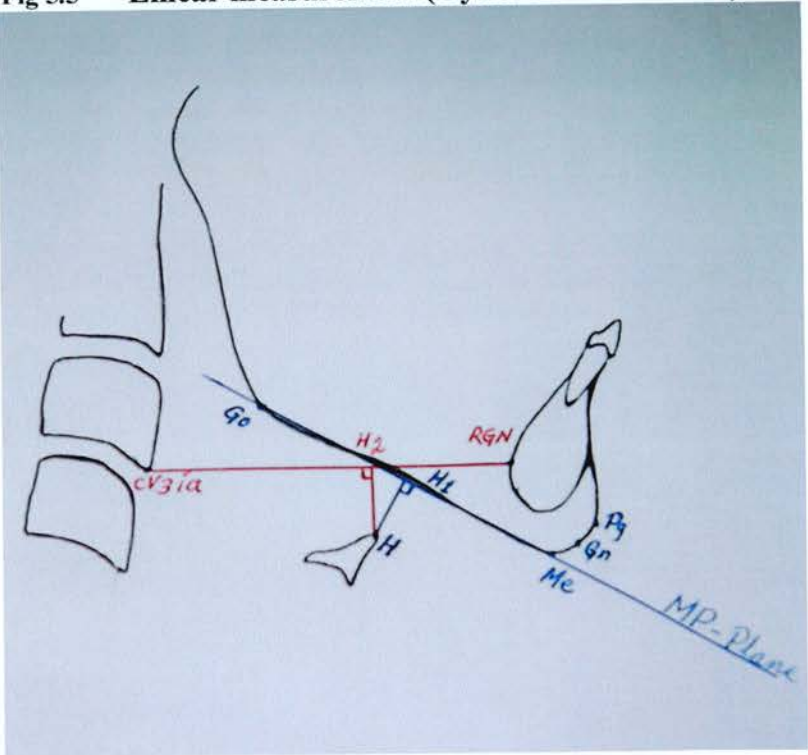


Table 5.7 Linear measurements (Hyoid bone variables definition)

Variables	Description
H-H1	The linear distance along a perpendicular from hyoid (H) to the Mandibular plane (H1).
H-H2	The linear distance between hyoid (H) and a perpendicular to the cv3ia-RGN plane.
(H-H1) + (H-H2)	Vertical Hyoid Position.

5.4 Method Error

Houston (1983) points out that any recorded measurements actually represent the 'True' value + Random error + Systemic error.

5.4.1 Random Error

Random error is defined as variability due to chance, and may act to attenuate a real correlation between cephalometric measurements such as those made during this investigation. In an effort to reduce the impact of such variability upon the data presented here, radiographs were all taken and subsequently analyzed maintaining a strict adherence standardized protocol, and the sample size was made as large as was practical, in order to reduce the 'net' effect of any errors upon results as indicated by the data. Houston (1983) suggests that quite possibly the greatest source of random error in any investigation involving cephalometric analysis is due to difficulty in radiographic landmark identification, for this reason a black thick paper with a whole in the middle is used to define the landmark.

5.4.2 Systemic Error

Systemic error is defined as the tendency to overestimate or to underestimate a parameter resulting in a 'biased' or unrepresentative sample. In the present situation such bias may occur through structural or methodological deficiencies in the study or through the investigator subconsciously weighting results. In an effort to minimize the impact of such bias, patients were selected from clinic records in order of their presentation for assessment / data of radiography, from November 2000. Only edentulous candidates and those found to have radiographs unsuitable for this investigation. (i.e. essential landmarks not visible), were excluded.

Tracing was performed only after the 'masking' of identifying markings such as the name and clinic number of the patient, so as to reduce the probability of subjective bias. All tracings and measurements were made by the author and adjusted for the measured degree of magnification, (determined through the inclusion of metal ruler in exposure, Fig. 5.1)

5.4.3 Calculations Error

An evaluation of method error was undertaken using the protocol as recommended by Houston (1983). From the investigated population group, twenty-five radiographs were randomly selected and both tracing and subsequent measurement was repeated for each case, with a minimum interval of a week between initial and repeated tracing.

Analysis of initial and repeated measurements is outlined in (Table 5.8). Systemic error was determined according to Houston's recommendations (1983) and the 't' value for each variable were calculated. Subsequently 't' value which would correspond to $P=0.05$ and $P=0.1$ were calculated. Houston suggests that no evidence of systemic error exists if $P>0.1$, and this is found to be the case for all reproduced variables.

Table 5.8 Analysis of initial and repeated measurements, n=25 (Black= angular, Blue= Linear)

Variables	No.	Mean	Std. Deviation	Std. Error of the Mean	df	t	95% Confidence Interval of the Difference	
							Lower	Upper
NSL/OPT	25	104.6000	8.1202	1.6240	24	64.407	101.2481	107.9519
FH/OPT	25	97.0400	6.4290	1.2858	24	75.471	94.3863	99.6937
NL/OPT	25	97.4200	6.4754	1.2951	24	75.223	94.7471	100.0929
NSL/CVT	25	111.3600	7.7815	1.5563	24	71.554	108.1479	114.5721
FH/CVT	25	104.1600	6.5459	1.3092	24	79.562	101.4580	106.8620
NL/CVT	25	104.5800	6.2261	1.2452	24	83.985	102.0100	107.1500
CVT/OPT	25	6.7600	2.7123	.5425	24	12.462	5.6404	7.8796
NL/NSL	25	7.7000	3.6228	.7246	24	10.627	6.2046	9.1954
MP/NSL	25	36.1600	4.3463	.8693	24	41.599	34.3660	37.9540
NL/MP	25	28.8400	5.4900	1.0980	24	26.266	26.5738	31.1062
FH/NSL	25	9.0600	3.6609	.7322	24	12.374	7.5488	10.5712
U1/L1	25	83.8000	8.4496	1.6899	24	49.588	80.3122	87.2878
U1/NL	25	79.9800	8.5434	1.7087	24	46.808	76.4535	83.5065
L1/MP	25	4.0200	2.8412	.5682	24	7.074	2.8472	5.1928
SNA	25	134.1600	15.5018	3.1004	24	43.272	127.7612	140.5588
SNB	25	106.4800	7.8865	1.5773	24	67.507	103.2246	109.7354
ANB	25	90.5000	9.6631	1.9326	24	46.828	86.5113	94.4887
N-NL	25	52.0600	3.5276	.7055	24	73.789	50.6039	53.5161
Gn-NL	25	66.3600	4.9927	.9985	24	66.456	64.2991	68.4209
S-NL	25	43.1200	3.5422	.7084	24	60.865	41.6578	44.5822
Go-NL	25	34.1800	4.5982	.9196	24	37.167	32.2820	36.0780
N-S	25	71.0600	3.7370	.7474	24	95.077	69.5175	72.6025
ANS-PNS	25	51.8000	4.8755	.9751	24	53.122	49.7875	53.8125
Me-Go	25	68.4600	3.8431	.7686	24	89.069	66.8737	70.0463
Overbite	25	3.7600	3.1824	.6365	24	5.908	2.4464	5.0736
Overjet	25	3.1600	2.1924	.4385	24	7.207	2.2550	4.0650
H-H1	25	21.2200	6.2518	1.2504	24	16.971	18.6394	23.8006
H-H2	25	10.3000	5.1031	1.0206	24	10.092	8.1935	12.4065
(H-H1)+(H-H2)	25	31.5200	10.3787	2.0757	24	15.185	27.2359	35.8041

Data analysis

All data was entered and analyzed using SPSS version 10.0 for Windows (SPSS Inc, Chicago, IL, USA, and Microsoft Excel 2003). Evaluation of frequency histograms reveals that all variables display sufficiently 'normal' distribution and hence multivariate analysis and 't' test procedures were utilized for data analysis. Although a normal distribution of subject population age is not an unusual finding, it may be explained in the present situation by the fact that OSAHS is a condition affecting primarily the 'middle' aged and the 'elderly'.

The relationships existing between the measurement pertaining to the angles and lines formed (between the OSAHS and the control groups) were analyzed to determine the correlation coefficients and 't' test. All tests were performed at the 95% level of significance, and consequently a p value less than 0.05 supported of the 'alternative' hypothesis in each case.

RESULTS

Measured variables were compared statistically using Multivariate analysis and one sample 't' test.

The descriptive lateral cephalometric data will be presented under angular and linear measurements headings.

6.1 ANGULAR MEASUREMENTS (17 variables)

- Cranio-cervical angulations (NSL/OPT, FH/OPT, NL/OPT, NSL/CVT, FH/CVT, NL/CVT)
- Cervical curvature (CVT/OPT)
- Maxillary inclination (NL/NSL)
- Mandibular inclination (MP/NSL)
- Maxillary mandibular relationship (NL/MP)
- Frankfurt Horizontal to anterior cranial base (FH/NSL)
- Facio-skeletal (SNA)
- Facio-skeletal (SNB)
- Facio-skeletal (ANB)
- Upper incisor to lower incisor (U1/L1)
- Upper incisor to maxillary plane (U1/NL)
- Lower incisor to mandibular plane (L1/MP)

Table 6.1 Angular Measurements (Multivariate analysis)
Descriptive Statistics

Group		Mean	Std. Deviation	N
NSL/OPT	control	99.0667	8.70566	30
	sample	103.8154	7.98953	65
	Total	102.3158	8.47150	95
FH/OPT	control	91.2500	8.55182	30
	sample	96.5385	7.17162	65
	Total	94.8684	7.98043	95
NL/OPT	control	90.4667	7.86408	30
	sample	95.8462	7.94951	65
	Total	94.1474	8.27193	95
NSL/CVT	control	110.000	8.40874	30
	sample	110.262	7.00060	65
	Total	110.182	7.42947	95
FH/CVT	control	102.183	8.29362	30
	sample	103.138	6.09385	65
	Total	102.836	6.83374	95
NL/CVT	control	101.400	7.56626	30
	sample	102.458	7.04657	65
	Total	102.121	7.19105	95
OPT/CVT	control	10.6000	4.41861	30
	sample	6.4615	3.17498	65
	Total	7.7684	4.07758	95
NL/NSL	control	8.7833	2.42360	30
	sample	8.4077	3.60001	65
	Total	8.5263	3.26601	95
MP/NSL	control	36.3500	6.42751	30
	sample	36.2000	6.18706	65
	Total	36.2474	6.23002	95
NL/MP	control	26.7167	6.76793	30
	sample	28.3385	6.24006	65
	Total	27.8263	6.42004	95
FH/NSL	control	8.1000	3.92472	30
	sample	8.2538	3.17476	65
	Total	8.2053	3.40876	95

Continued Table 6.1
Angular Measurements (Multivariate analysis)
Descriptive Statistics

Group		Mean	Std. Deviation	N
SNA	control	76.2500	18.99217	30
	sample	82.3077	6.45700	65
	Total	80.3947	12.15238	95
ANB	control	4.0333	3.70446	30
	sample	4.1615	3.78020	65
	Total	4.1211	3.73719	95
U1/L1	control	132.1500	12.07530	30
	sample	136.7692	14.01229	65
	Total	135.3105	13.53977	95
U1/NL	control	107.8000	9.17230	30
	sample	106.4615	7.89645	65
	Total	106.8842	8.29459	95
L1/MP	control	92.5000	9.10002	30
	sample	88.7077	9.05793	65
	Total	89.9053	9.19508	95
sqrt/SNB	control	8.7677	.21283	30
	sample	8.8314	.32967	65
	Total	8.8113	.29808	95

Due to the lack of Normality, variable SNB has been transformed by the square root function (ie, it has been replaced in the analysis by the square root of SNB).

	NSL/OPT	FH/OPT	NL/OPT	NSL/CVT	FH/CVT	NL/CVT	OPT/CVT	NL/NSL	MP/NSL	NL/MP	FH/NSL	SNA	SNB	ANB	U1/L1	U1/NL
FH/OPT	0.889 0.000															
NL/OPT	0.901 0.000	0.856 0.000														
NSL/CVT	0.860 0.000	0.704 0.000	0.731 0.000													
FH/CVT	0.757 0.000	0.836 0.000	0.699 0.000	0.863 0.000												
NL/CVT	0.754 0.000	0.670 0.000	0.843 0.000	0.869 0.000	0.811 0.000											
OPT/CVT	-0.506 0.000	-0.552 0.000	-0.520 0.000	-0.011 0.919	-0.040 0.703	-0.013 0.903										
NL/NSL	0.200 0.052	0.073 0.480	-0.187 0.070	0.289 0.005	0.156 0.131	-0.170 0.099	0.067 0.522									
MP/NSL	0.198 0.054	0.075 0.468	0.087 0.404	0.245 0.017	0.120 0.247	0.117 0.259	0.001 0.995	0.350 0.000								
NL/MP	0.075 0.471	0.046 0.659	0.143 0.166	0.061 0.559	0.036 0.733	0.149 0.150	-0.052 0.615	-0.105 0.313	0.773 0.000							
FH/NSL	0.344 0.001	0.003 0.980	0.256 0.012	0.390 0.000	-0.003 0.976	0.290 0.004	-0.026 0.804	0.293 0.004	0.288 0.005	0.046 0.655						
SNA	-0.040 0.700	0.020 0.845	0.042 0.688	-0.269 0.008	-0.220 0.032	-0.183 0.075	-0.250 0.015	-0.205 0.047	-0.169 0.101	-0.028 0.790	-0.117 0.257					
SNB	-0.067 0.521	0.051 0.625	0.084 0.418	-0.176 0.088	-0.058 0.578	-0.000 0.998	-0.151 0.143	-0.398 0.000	-0.348 0.001	-0.132 0.203	-0.229 0.026	0.501 0.000				
ANB	-0.010 0.924	-0.074 0.474	-0.062 0.551	-0.083 0.424	-0.160 0.121	-0.169 0.101	-0.149 0.151	0.198 0.055	0.335 0.001	0.270 0.008	0.105 0.311	0.115 0.269	-0.264 0.010			
U1/L1	0.206 0.046	0.265 0.009	0.233 0.023	0.173 0.093	0.271 0.008	0.188 0.067	-0.104 0.318	0.004 0.970	-0.087 0.404	-0.021 0.842	0.019 0.857	-0.055 0.593	0.037 0.725	-0.236 0.021		
U1/NL	-0.246 0.016	-0.245 0.017	-0.306 0.003	-0.234 0.023	-0.260 0.011	-0.295 0.004	0.073 0.484	0.044 0.669	-0.244 0.017	-0.298 0.003	-0.135 0.193	0.069 0.505	0.096 0.356	-0.081 0.433	-0.684 0.000	
L1/MP	-0.243 0.018	-0.281 0.006	-0.257 0.012	-0.171 0.098	-0.238 0.020	-0.178 0.085	0.200 0.052	-0.036 0.732	-0.240 0.019	-0.269 0.008	-0.038 0.716	0.059 0.568	0.003 0.975	0.173 0.093	-0.725 0.000	0.441 0.000
	NSL/OPT	FH/OPT	NL/OPT	NSL/CVT	FH/CVT	NL/CVT	OPT/CVT	NL/NSL	MP/NSL	NL/MP	FH/NSL	SNA	SNB	ANB	U1/L1	U1/NL

Table. 6.2 Correlation statistics

Discussion of correlation results

Due to the large number of tests, only those with a correlation of $p<0.01$ will be reported. Correlations highlighted in red are significant. The closer the correlation coefficient is to ± 1 , the better the relationship, regardless of the p-value.

As would be expected, the 6 craniocervical measures are all highly correlated ($p<0.001$). Of the other variables, OPT/CVT is highly correlated with NSL/OPT, FH/OPT and NL/OPT but not in the least related to the other three craniocervical variables. Many of the comparisons with the same start point are correlated, for example, NL/MP with MP/NSL has a correlation coefficient (ρ) of 0.773 and $p<0.001$. SNA does not appear to be highly related to any other variables, as even the sole significant correlation is only -0.269.

Table 6.3 Angular Measurements Multivariate Tests(c)

This simultaneously tests each factor effect (group) on the dependent variables. Wilks' Lambda is the usual test to quote when there are more than two dependent variables, although for each test the F-statistic is the same. Hence, there is a statistically significant difference between the sample and control patients ($p=0.011$).

Effect		Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power(a)
Intercept	Pillai's Trace	1.000	23546.626(b)	17.000	77.000	.000	1.000	400292.634	1.000
	Wilks' Lambda	.000	23546.62 (b)	17.000	77.000	.000	1.000	400292.634	1.000
	Hotelling's Trace	5198.606	23546.626(b)	17.000	77.000	.000	1.000	400292.634	1.000
	Roy's Largest Root	5198.606	23546.626(b)	17.000	77.000	.000	1.000	400292.634	1.000
Group	Pillai's Trace	.325	2.185(b)	17.000	77.000	.011	.325	37.141	.966
	Wilks' Lambda	.675	2.185(b)	17.000	77.000	.011	.325	37.141	.966
	Hotelling's Trace	.482	2.185(b)	17.000	77.000	.011	.325	37.141	.966
	Roy's Largest Root	.482	2.185(b)	17.000	77.000	.011	.325	37.141	.966

a Computed using alpha = .05

b Exact statistic

c Design: Intercept+Group

Table 6.4 Angular Measurements (Parameter Estimates)

This allows you to assess the significance of the factor 'group' on each of the dependent variables. For example, for the variable NSL/OPT 'control' is statistically significantly different from 'sample' ($p=0.01$). 'Sample' is set to be the reference category, which is why the coefficient (B) is set to 0.

Dependent Variable	Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared	Noncent. Parameter	Observed Power(a)
						Lower Bound	Upper Bound			
NSL/OPT	Intercept	103.815	1.020	101.829	.000	101.791	105.840	.991	101.829	1.000
	[Group=control]	-4.749	1.814	-2.617	.010	-8.351	-1.146	.069	2.617	.736
	[Group=sample]	0(b)
FH/OPT	Intercept	96.538	.946	102.023	.000	94.659	98.418	.991	102.023	1.000
	[Group=control]	-5.288	1.684	-3.141	.002	-8.632	-1.945	.096	3.141	.875
	[Group=sample]	0(b)
NL/OPT	Intercept	95.846	.983	97.531	.000	93.895	97.798	.990	97.531	1.000
	[Group=control]	-5.379	1.749	-3.076	.003	-8.852	-1.907	.092	3.076	.861
	[Group=sample]	0(b)
NSL/CVT	Intercept	110.269	.926	119.040	.000	108.430	112.109	.993	119.040	1.000
	[Group=control]	-.269	1.648	-.163	.871	-3.543	3.004	.000	.163	.053
	[Group=sample]	0(b)
FH/CVT	Intercept	103.131	.850	121.277	.000	101.442	104.819	.994	121.277	1.000
	[Group=control]	-.947	1.513	-.626	.533	-3.952	2.058	.004	.626	.095
	[Group=sample]	0(b)
NL/CVT	Intercept	102.454	.895	114.522	.000	100.677	104.230	.993	114.522	1.000
	[Group=control]	1.054	1.592	-.662	.510	-4.215	2.108	.005	.662	.100
	[Group=sample]	0(b)
OPT/CVT	Intercept	6.462	.448	14.434	.000	5.573	7.350	.691	14.434	1.000
	[Group=control]	4.138	.797	5.195	.000	2.557	5.720	.225	5.195	.999
	[Group=sample]	0(b)
NL/NSL	Intercept	8.408	.407	20.674	.000	7.600	9.215	.821	20.674	1.000
	[Group=control]	.376	.724	.519	.605	-1.061	1.813	.003	.519	.081
	[Group=sample]	0(b)

Continued Table 6.4 Angular Measurements (Parameter Estimates)

Dependent Variable	Parameter	B	Std. Error	T	Sig.	95% Confidence Interval		Partial Eta Squared	Noncent. Parameter	Observed Power(a)
						Lower Bound	Upper Bound			
MP/NSL	Intercept	36.200	.777	46.599	.000	34.657	37.743	.959	46.599	1.000
	[Group=control]	.150	1.382	.109	.914	-2.595	2.895	.000	.109	.051
	[Group=sample]	0(b)
NL/IMP	Intercept	28.338	.795	35.647	.000	26.760	29.917	.932	35.647	1.000
	[Group=control]	-1.622	1.415	-1.146	.255	-4.431	1.187	.014	1.146	.206
	[Group=sample]	0(b)
FH/NSL	Intercept	8.254	.425	19.422	.000	7.410	9.098	.802	19.422	1.000
	[Group=control]	-.154	.756	-.203	.839	-1.656	1.348	.000	.203	.055
	[Group=sample]	0(b)
SNA	Intercept	82.308	1.474	55.851	.000	79.381	85.234	.971	55.851	1.000
	[Group=control]	-6.058	2.622	-2.310	.023	-11.265	-.850	.054	2.310	.628
	[Group=sample]	0(b)
ANB	Intercept	4.162	.466	8.931	.000	3.236	5.087	.462	8.931	1.000
	[Group=control]	-.128	.829	-.155	.877	-1.775	1.518	.000	.155	.053
	[Group=sample]	0(b)
U1/L1	Intercept	136.769	1.667	82.054	.000	133.459	140.079	.986	82.054	1.000
	[Group=control]	-4.619	2.966	-1.557	.123	-10.509	1.271	.025	1.557	.338
	[Group=sample]	0(b)
U1/NL	Intercept	106.462	1.031	103.221	.000	104.413	108.510	.991	103.221	1.000
	[Group=control]	1.338	1.835	.729	.468	-2.306	4.983	.006	.729	.111
	[Group=sample]	0(b)
L1/IMP	Intercept	88.708	1.125	78.842	.000	86.473	90.942	.985	78.842	1.000
	[Group=control]	3.792	2.002	1.894	.061	-.184	7.768	.037	1.894	.466
	[Group=sample]	0(b)
Sqrt(SNB)	Intercept	8.831	.037	238.779	.000	8.758	8.905	.998	238.779	1.000
	[Group=control]	-.064	.066	-.967	.336	-.194	.067	.010	.967	.160
	[Group=sample]	0(b)

a Computed using alpha = .05
b This parameter is set to zero because it is redundant.

6.1.1 Cranio-cervical angulations

Descriptive data for the variables expressing the posture of the head and the cervical column for the OSAHS and the control are listed in tables 6.1, 6.2 and 6.3, 6.4 and expressed in figures 6.1, 6.2, 6.3, 6.4, 6.5 and 6.6.

The cranio-cervical angles were *larger* in the OSAHS group than that of the control and have shown significant correlation results with special high significances to NSL/OPT, FH/OPT and NL/OPT.

The ‘t’ test have shown significant result in relation to the angles formed with the OPT than those with the CVT (NSL/OPT $P=.01^{**}$, FH/OPT $P=.002^{***}$, NL/OPT $P=.003^{***}$).

($P<0.05^{*}$, $P<01^{**}$, $P<0.001^{***}$).

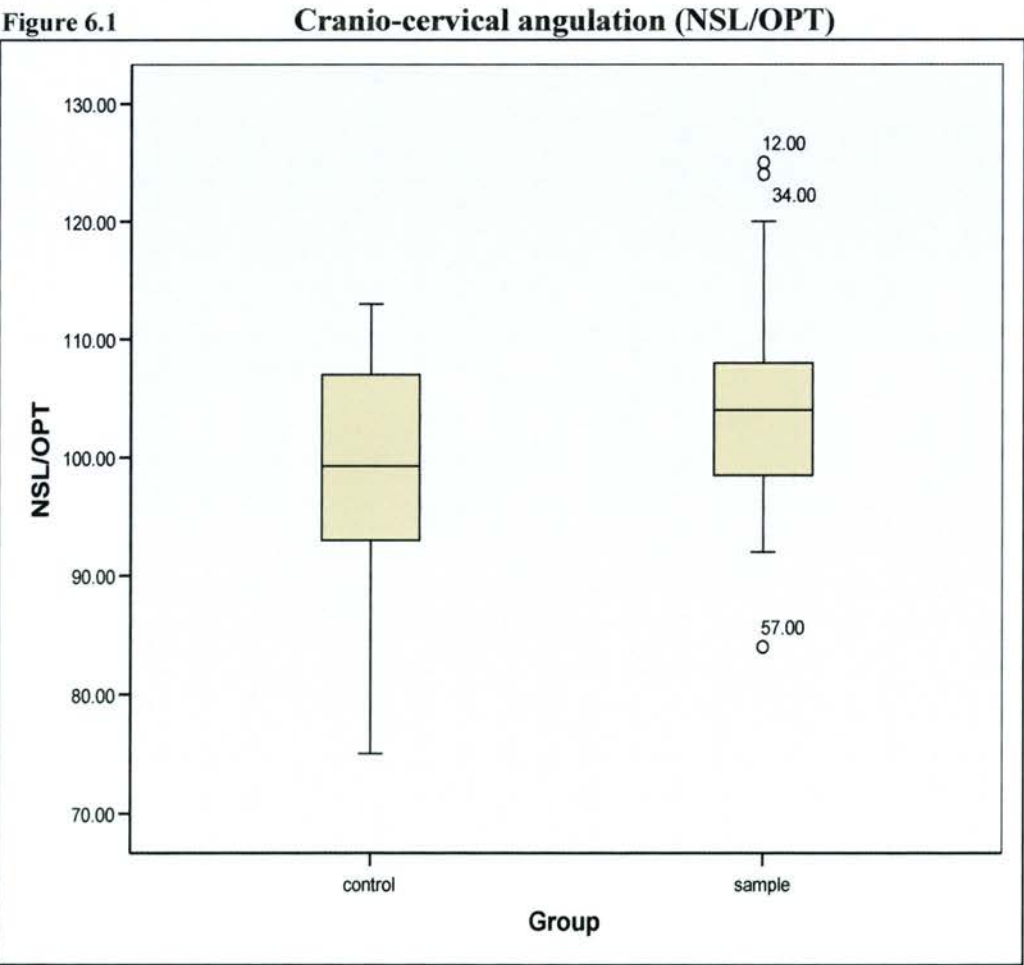


Figure 6.2 Cranio-vervical angulation (FH/OPT)

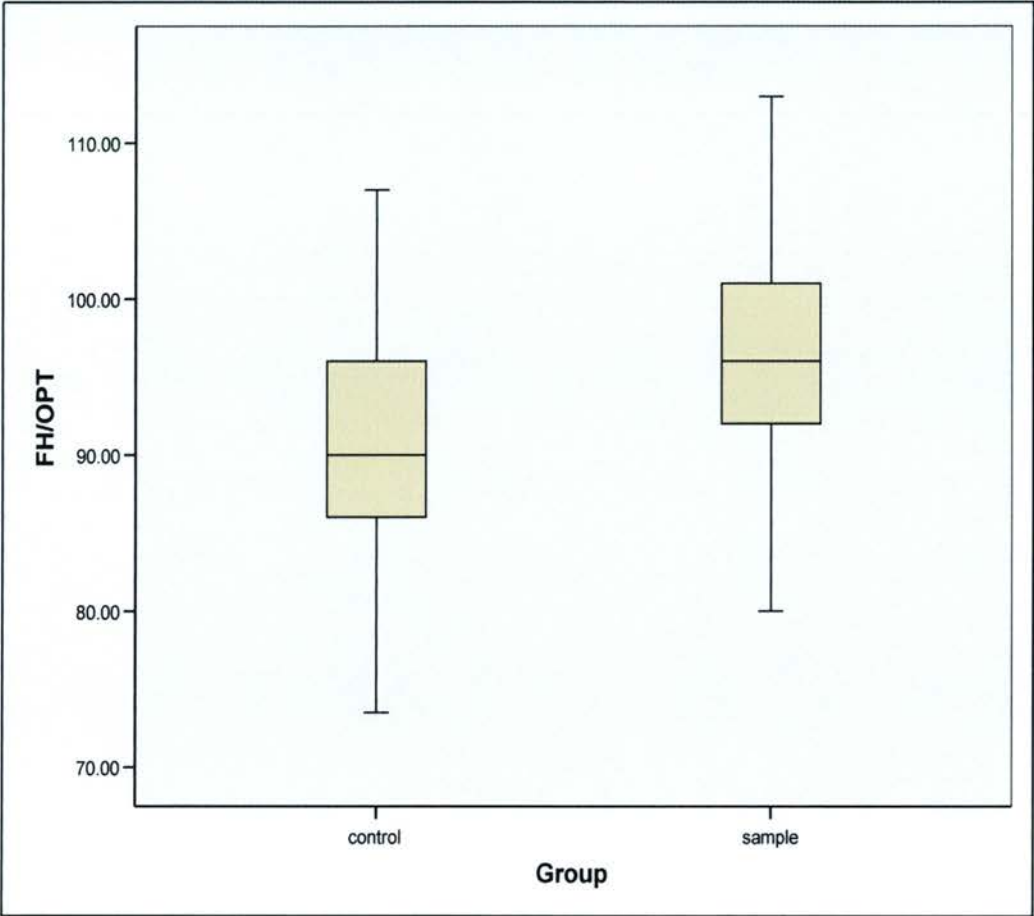


Figure 6.3 Cranio-cervical angulation (NL/OPT)

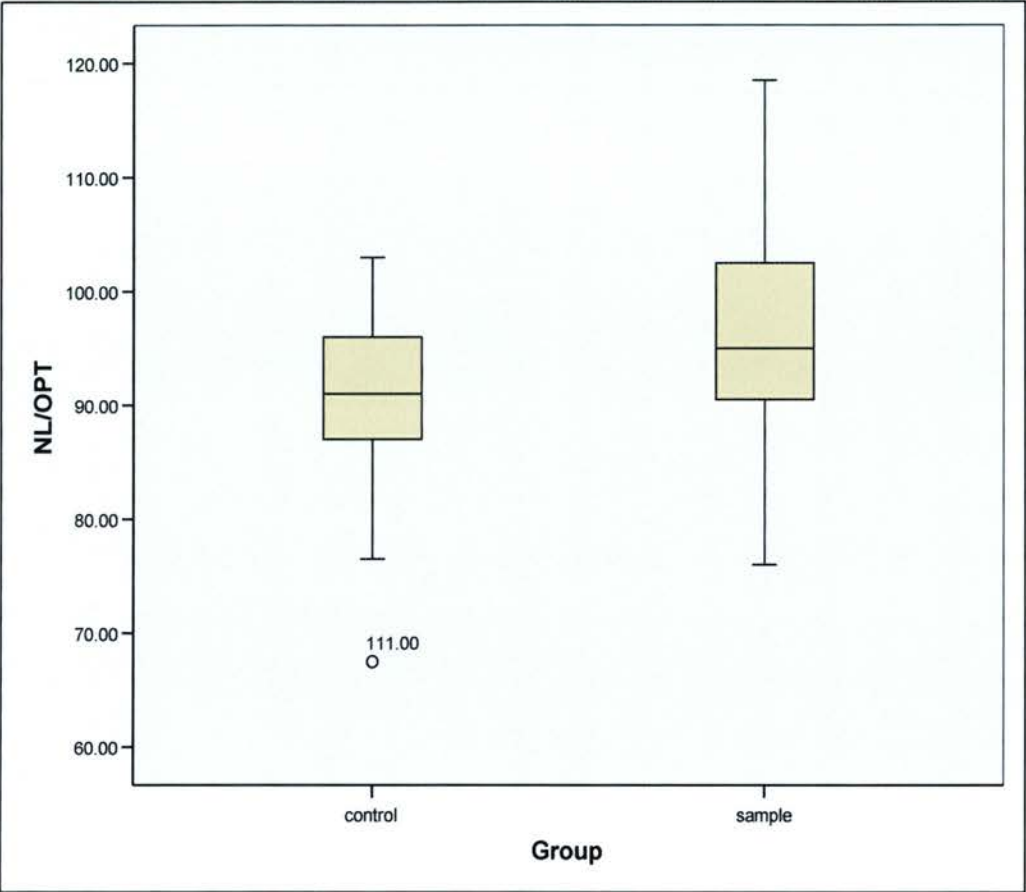


Figure 6.4 Cranio-cervical angulation (NSL/CVT)

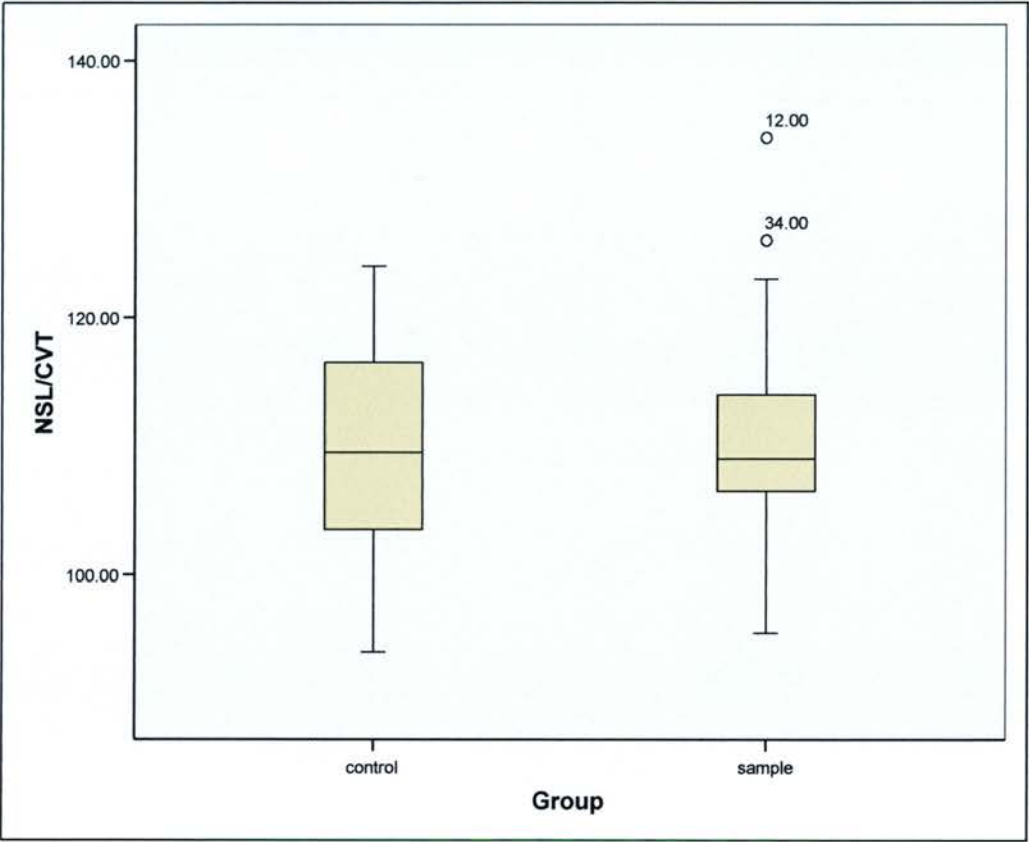


Figure 6.5 Cranio-cervical angulation (FH/CVT)

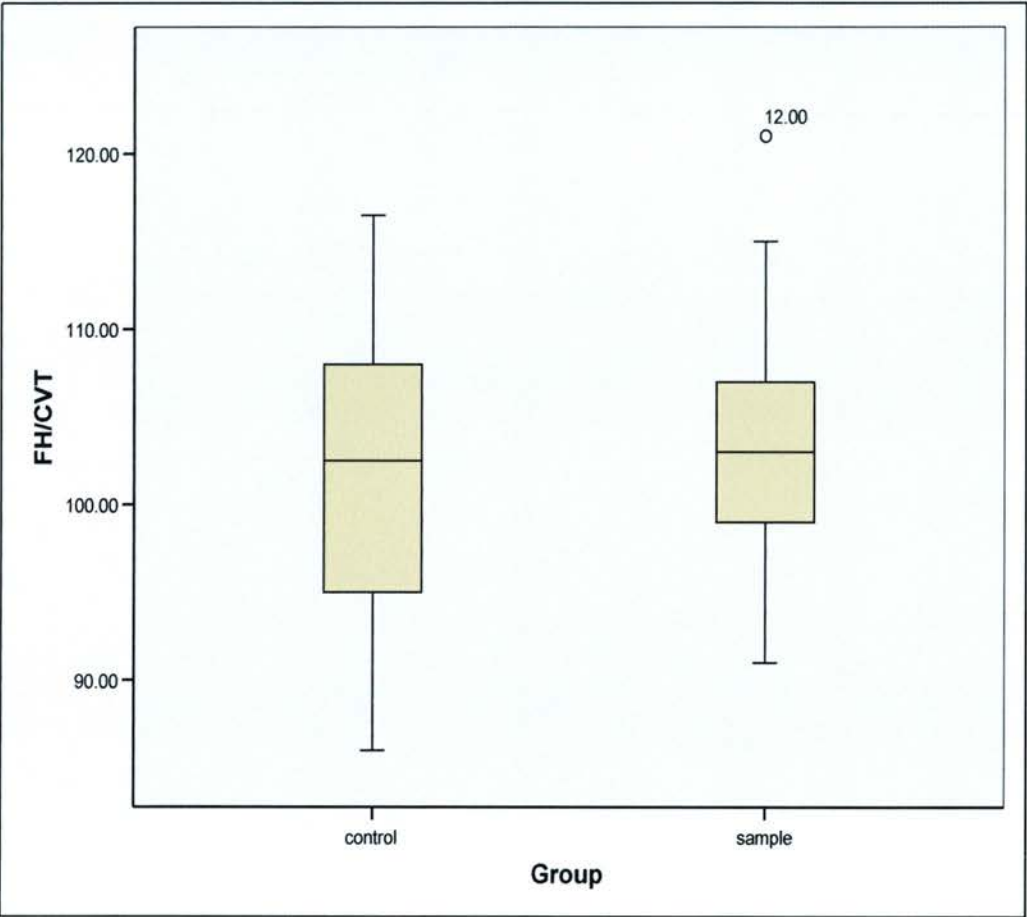
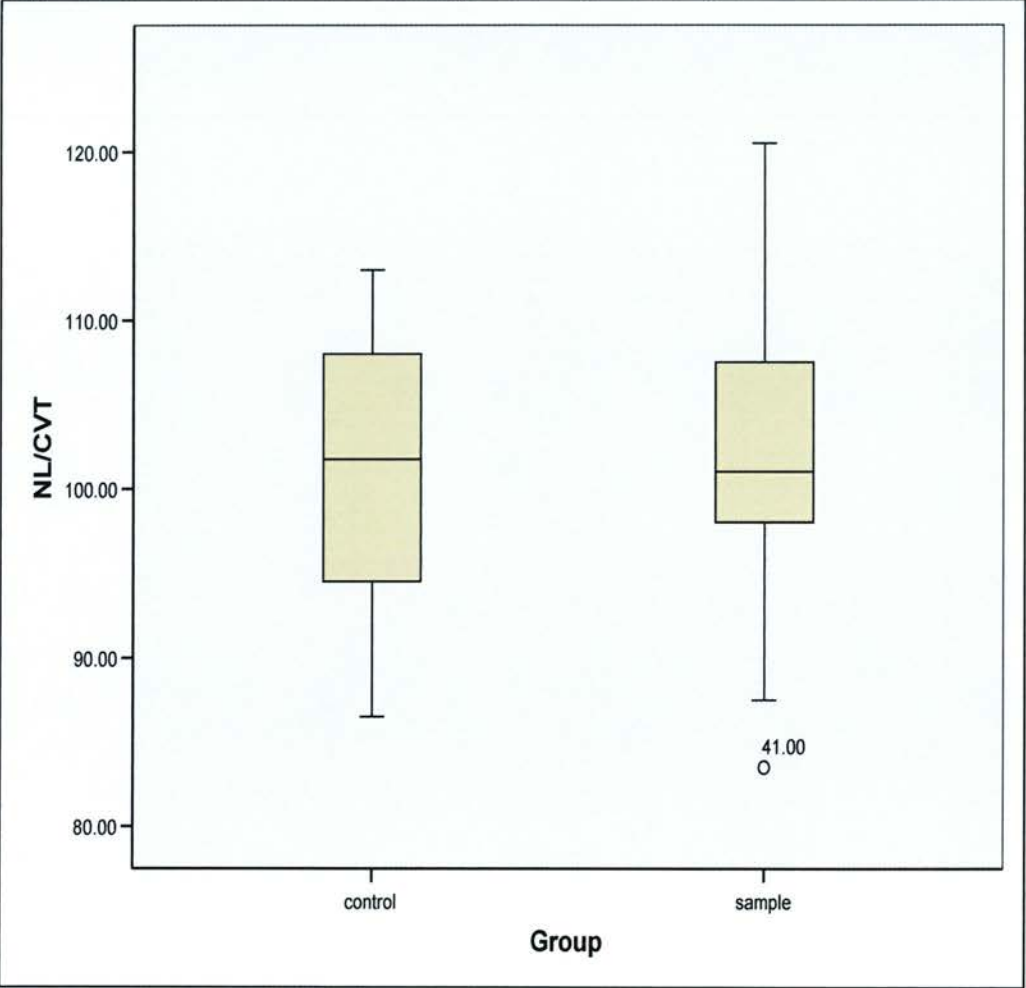


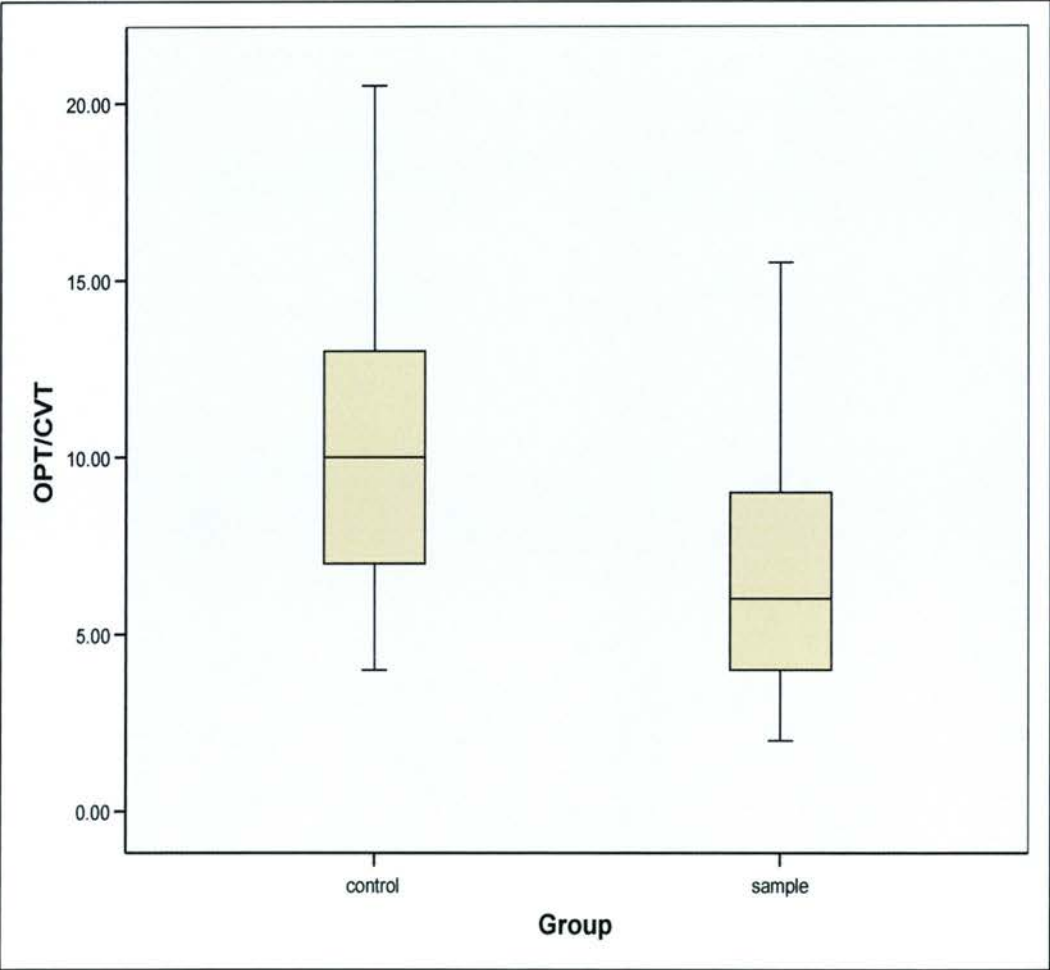
Figure 6.6 Cranio-cervical angulation (NL/CVT)



6.1.2 Cervical curvature

The angle of the cervical curvature (OPT/CVT) of the OSAHS group has shown to be *smaller* than that of the control group, mean 6.46° , 10.60 ° , SD 3.17498 and 4.41861 respectively, with a highly significant result $P=0.000***$ (Fig.6.7, tables 6.1, 6.2, 6.3, and 6.4).

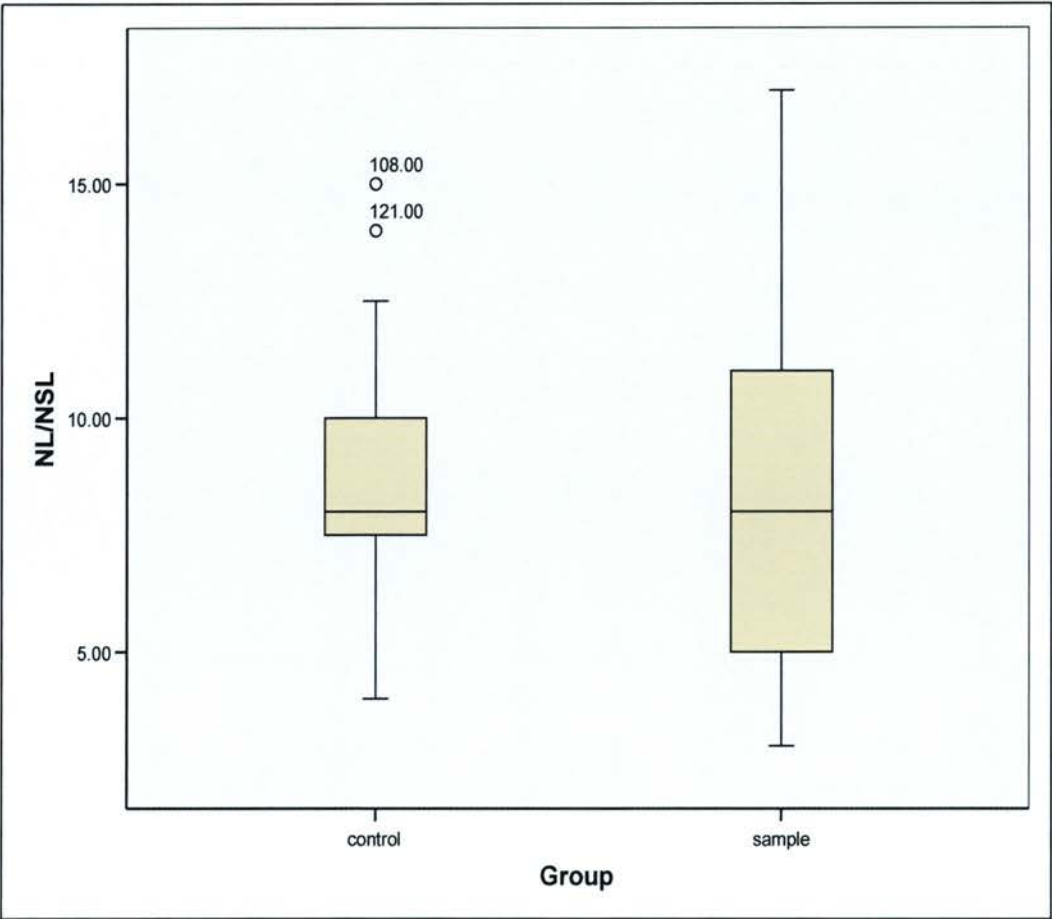
Figure 6.7 Cervical cutvature (OPT/CVT)



6.1.3 Maxillary inclination

NL/NSL has found to be *lower* in the OSAHS group than the control, mean 8.41°, 8.78°, SD 3.60001 and 2.42360 respectively, but statistically insignificant $P=0.605$ (Fig. 6.8, tables 6.1, 6.2, 6.3 and 6.4).

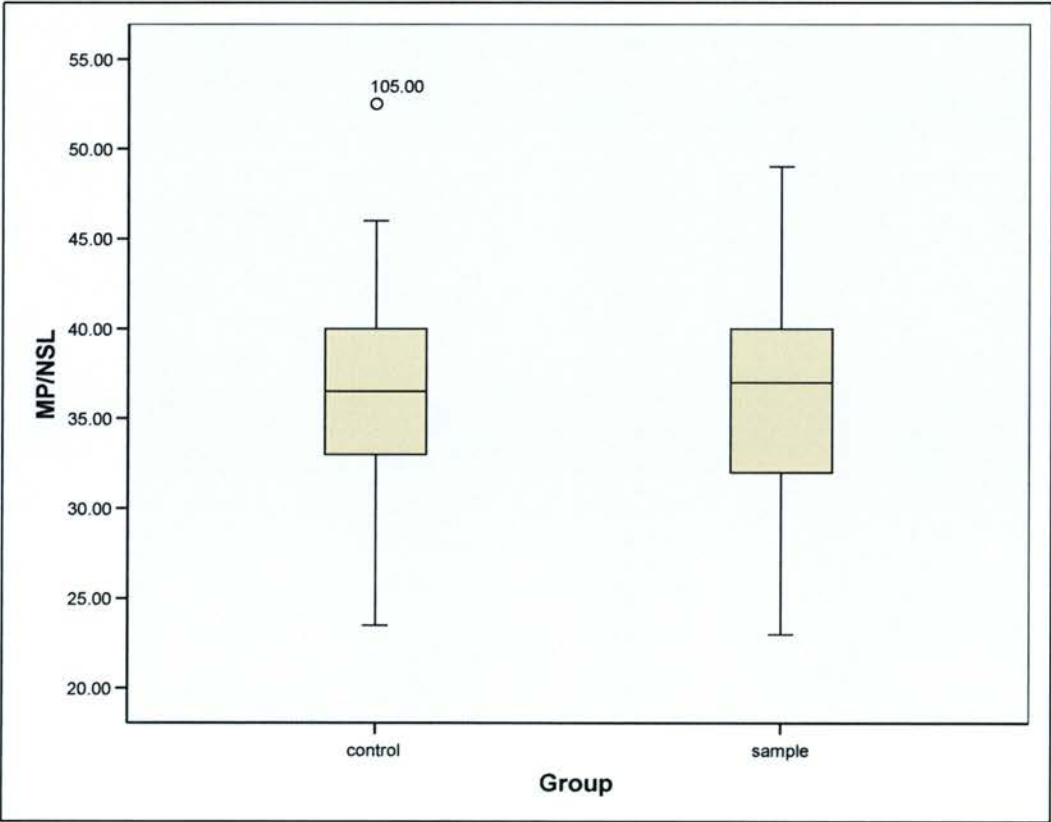
Figure 6.8 Maxillary inclination (NL/NSL)



6.1.4 Mandibular Inclination

MP/NSL has been found to be *lower* in OSAHS than that of the control group, mean 36.20°, 36.35°, SD 6.18706, 6.42751 respectively, but with insignificant result $P=0.914$ (Fig. 6.9 , tables 6.1, 6.2, 6.3 and 6.4).

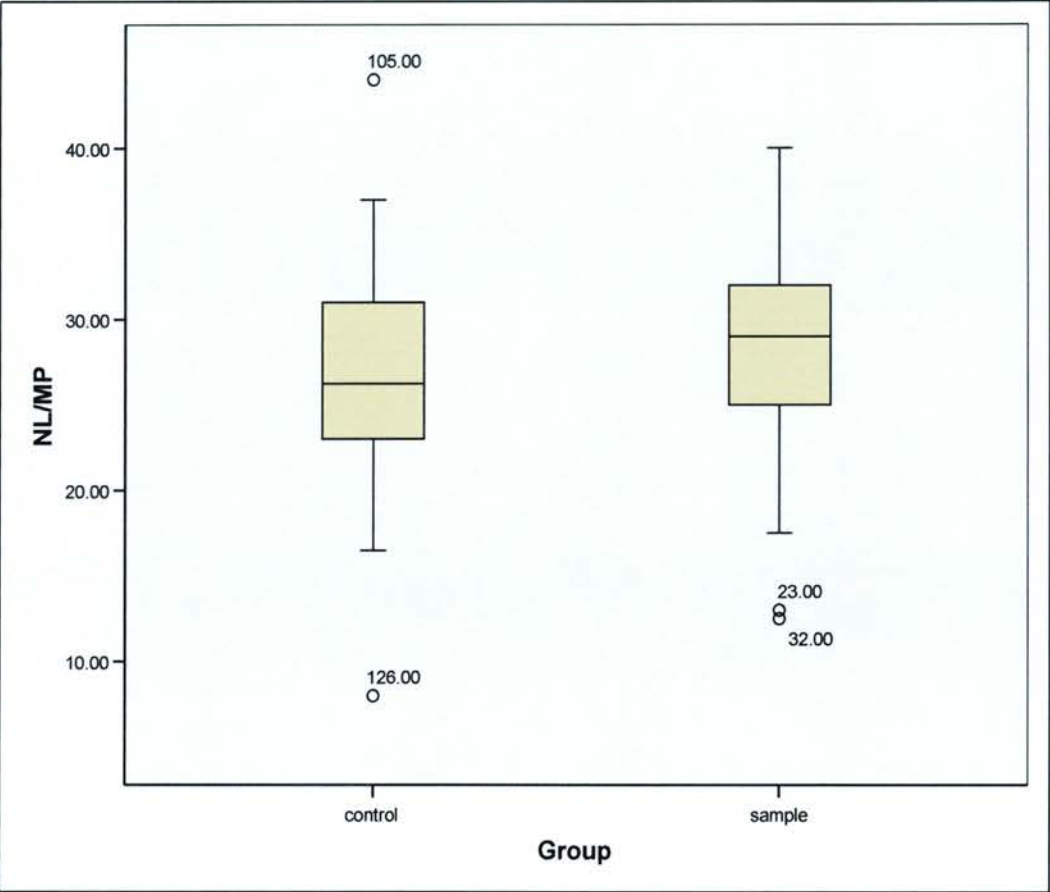
Figure 6.9 Mandibular inclination (MP/NSL)



6.1.5 Maxillary Mandibular Relationship (Inter-maxillary angle)

The NL/MP angle is found to be *higher* in OSAHS group than the control, mean 28.34°, 26.72°, SD 56.24006 and 6.76793 respectively, but with insignificant result $P=0.255$ (Fig. 6.10, tables 6.1, 6.2, 6.3 and 6.4).

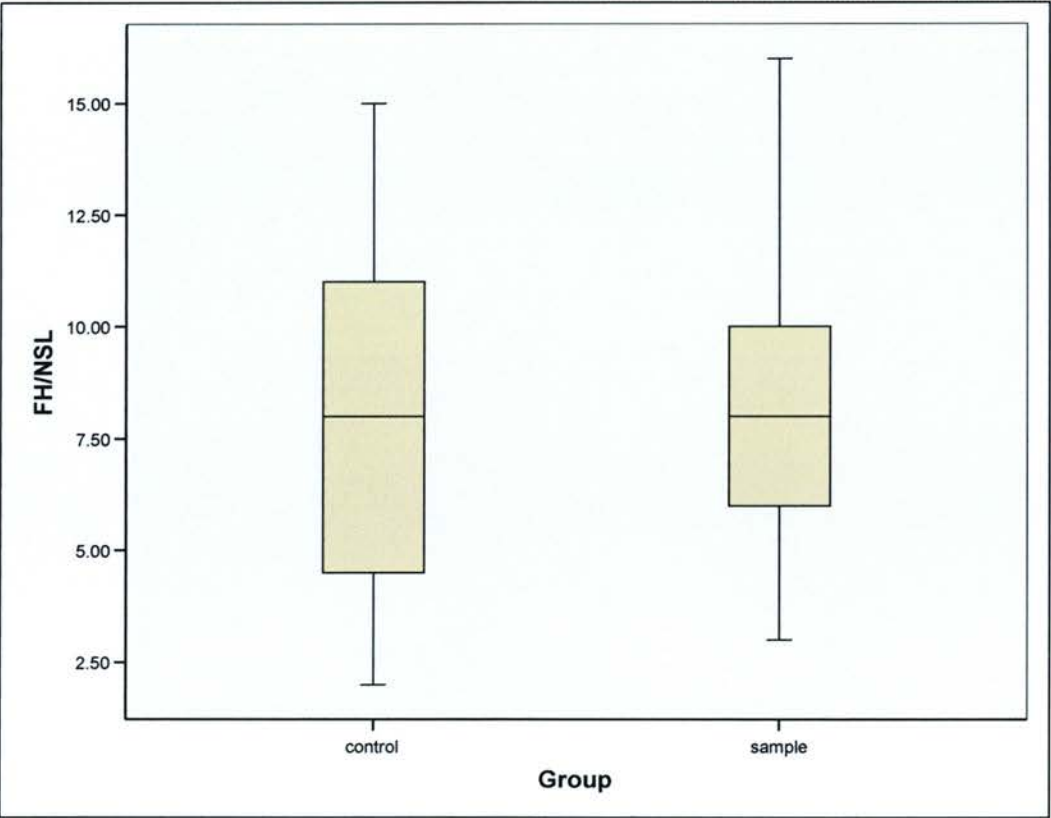
Figure 6.10 **Inter-maxillar angle (NL/MP)**



6.1.6 Frankfurt Horizontal to Nasion Sella Line

FH/NSL showed to be *higher* in OSAHS group than the control, mean 8.25°, 8.10°, SD 3.17476 and 3.92472 respectively, but shows insignificant result $P=0.839$ (Fig. 6.11, tables 6.1, 6.2, 6.3 and 6.4).

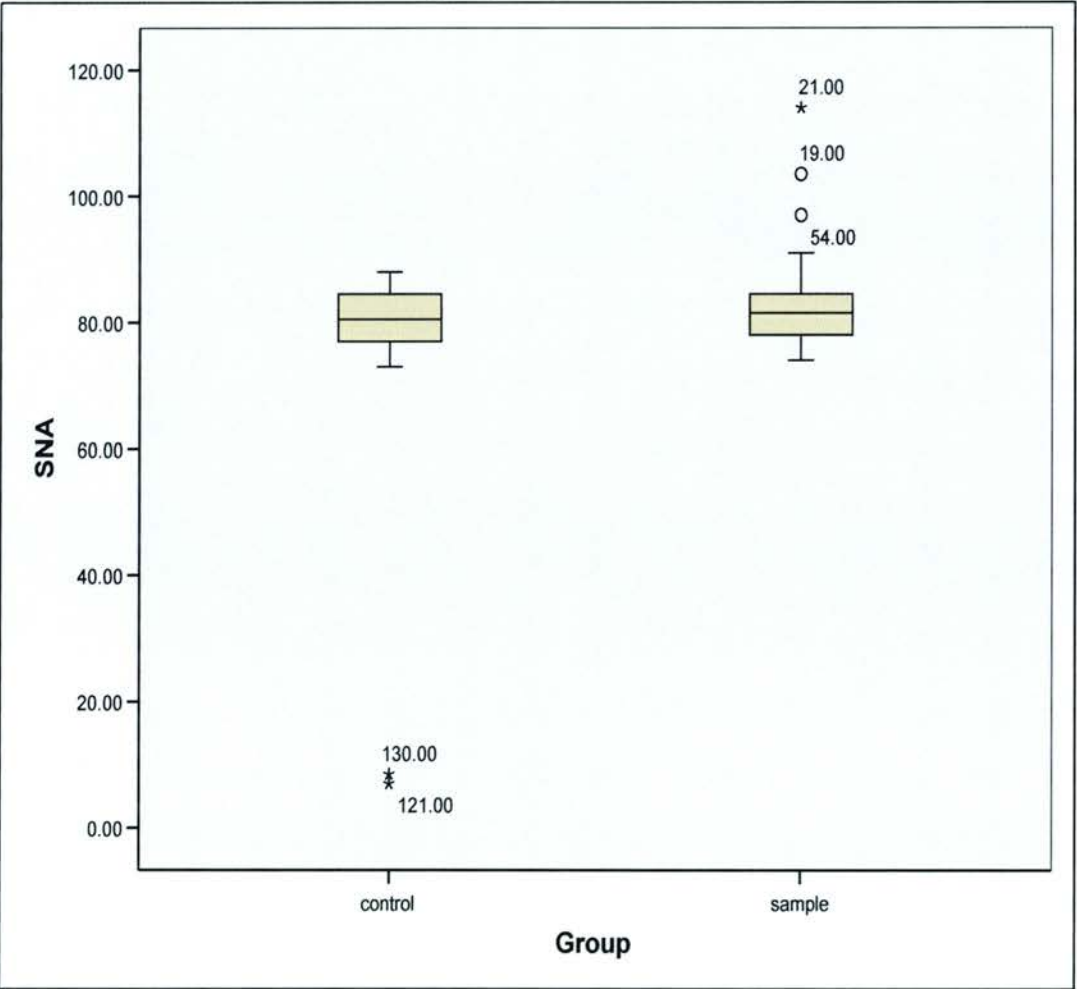
Figure 6.11 Frankfurt Horizontal to Nasion Sella Line (FH/NSL)



6.1.7 Facio-skeletal Relationship (SNA)

SNA angle appeared *higher* in the OSAHS group when compared to the control, mean 82.31°, 76.25°, SD 3.78020 and 3.70446 respectively, with statistically significant result $P=0.023^*$ (Fig. 6.12, tables 6.1, 6.2, 6.3 and 6.4).

Figure 6.12 **Facio-skeletal angle (SNA)**



6.1.8 Facio-skeletal Relationship (SNB)

SNB showed to be *higher* in the OSAHS group than the control, mean 79.17°, 76.93°, SD 8.089 and 3.709 respectively, but statistically insignificant result $P=0.336$ (Fig. 6.13a and b, tables 6.1, 6.2, 6.3 and 6.4).

Figure 6.13a **Facio-skeletal angle (SNB)**

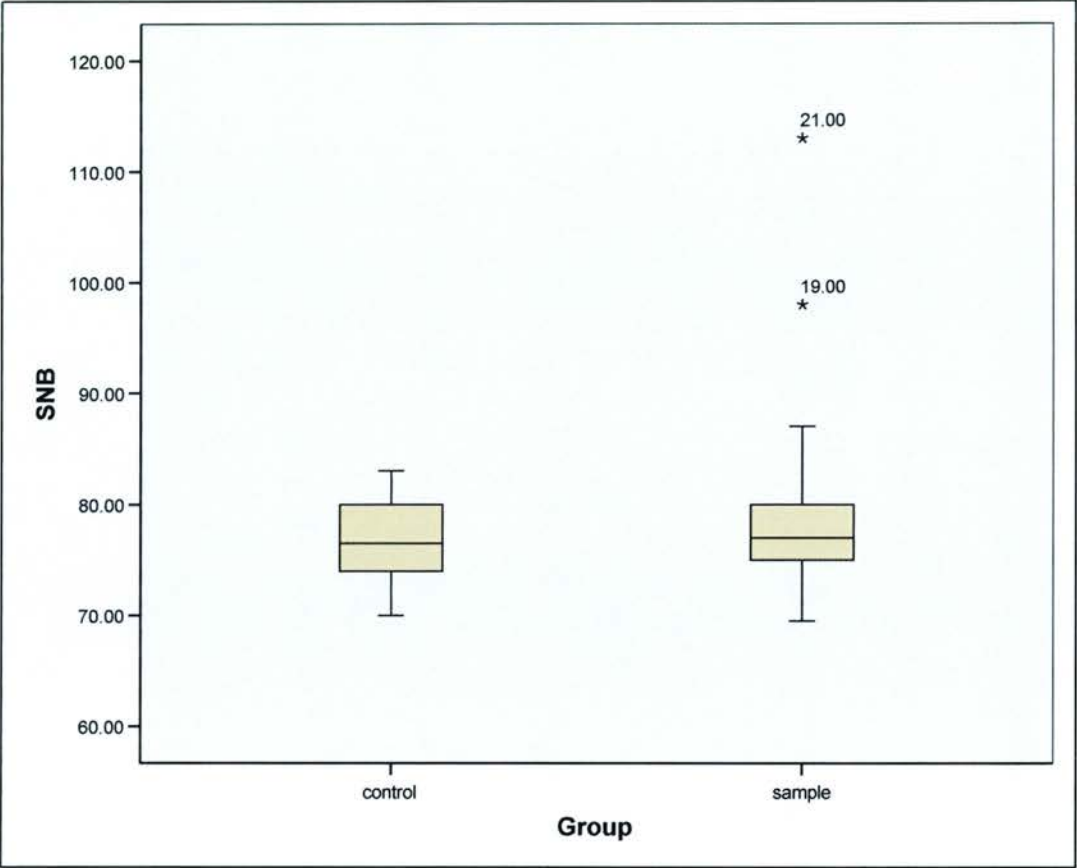
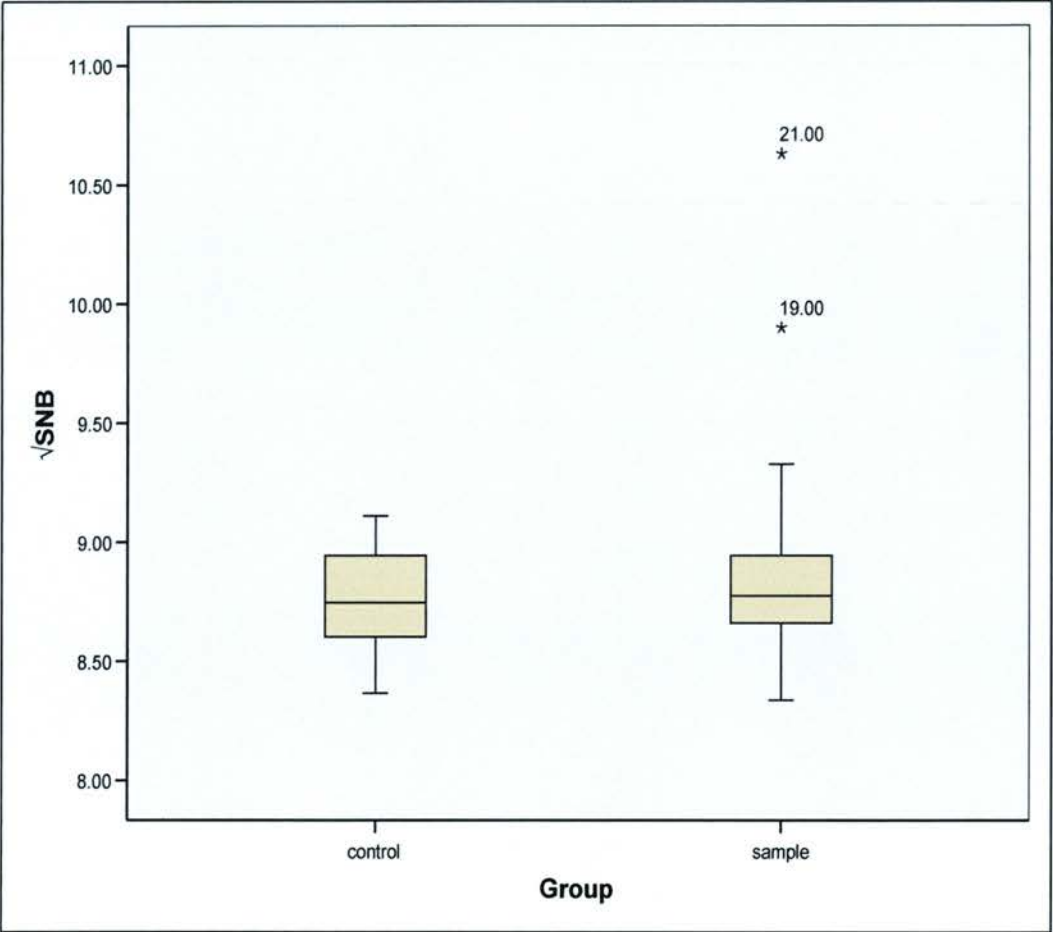


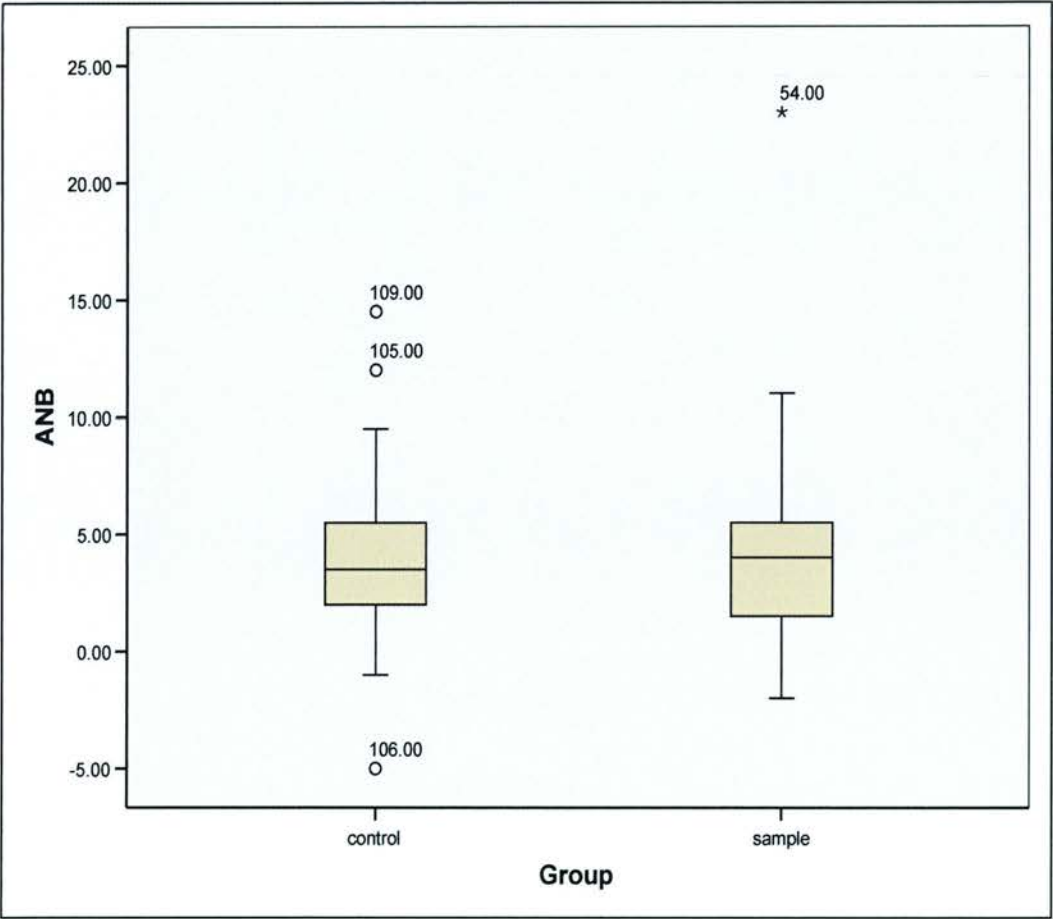
Fig. 6.13b **Facio-skeletal angle (Square root SNB)**



6.1.9 Facio-skeletal Relationship (ANB)

ANB angle appeared to be slightly *higher* in OSAHS than the control group, mean 4.16°, 4.03°, SD 3.78020, 3.70446, but with statistically insignificant result $P=0.877$ (Fig. 6.14, tables 6.1, 6.2, 6.3 and 6.4).

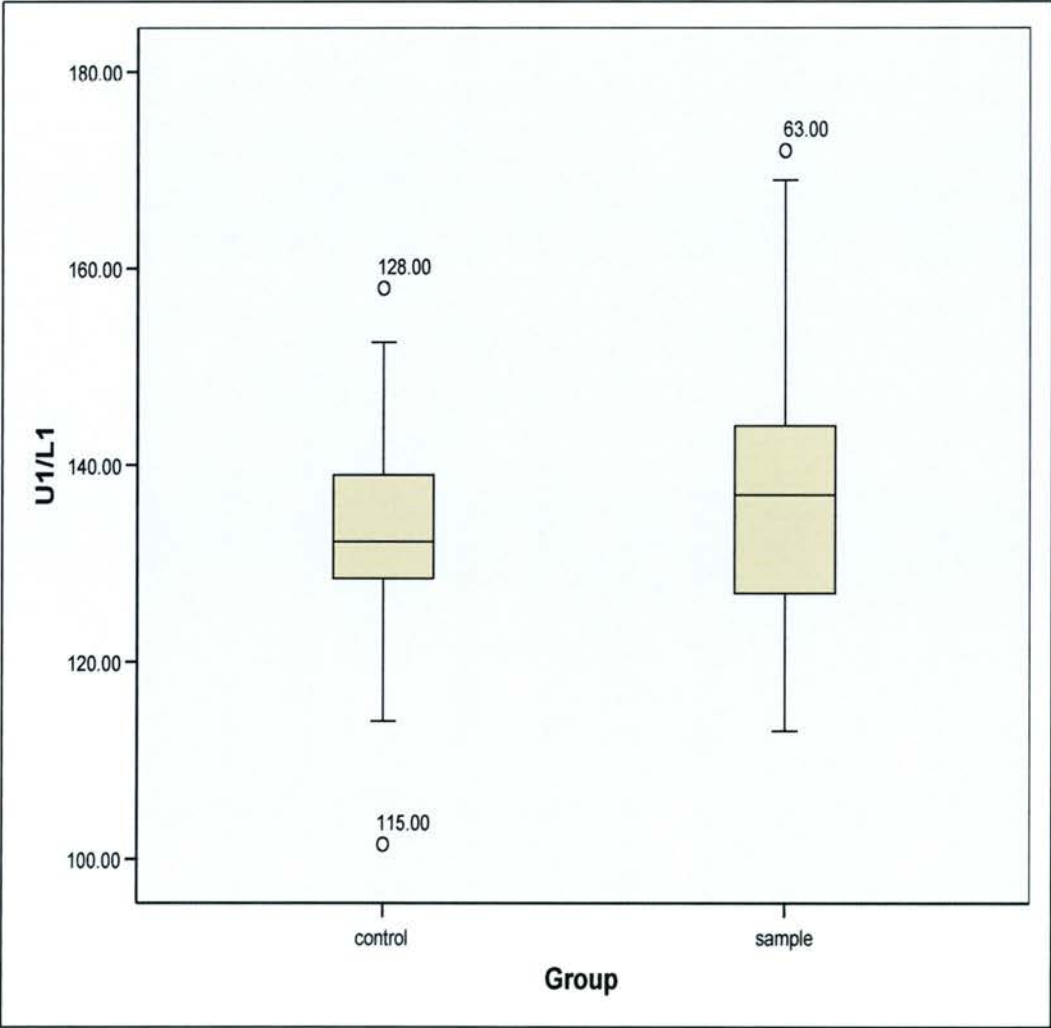
Figure 6.14 **Facio-skeletal angle (ANB)**



9.1.10 Upper Incisor to Lower Incisor

U1/L1 was found to be *higher* in the OSAHS group than the control, mean 136.77°, 132.15°, SD 14.01229 and 12.07530 respectively, but statistically insignificant result $P=0.123$ (Fig. 6.15, tables 6.1, 6.2, 6.3 and 6.4).

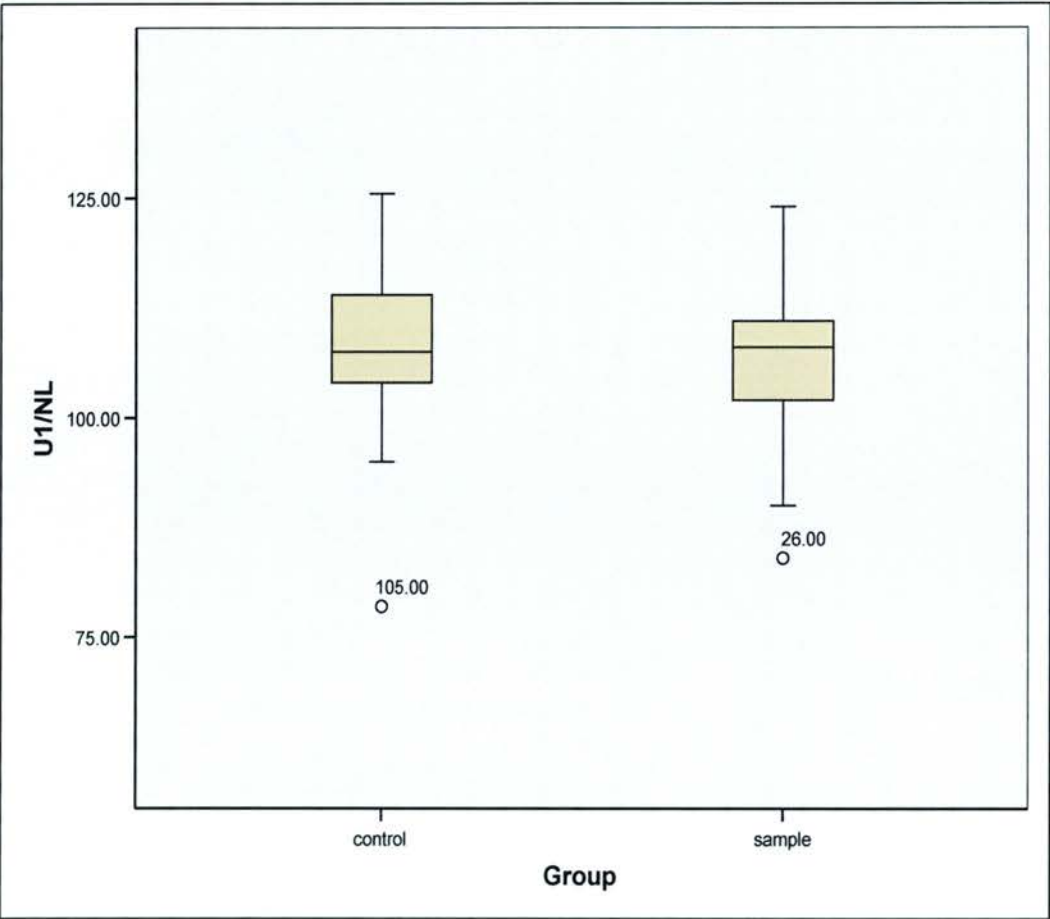
Table 6.15 Upper incisor to lower incisor angle (U1/L1)



6.1.11 Upper Incisor to Maxillary Plane

U1/NL has shown to be *reduced* in the OSAHS group than the control, mean 106.46°, 107.80°, SD 7.89645 and 9.17230 respectively, but statistically insignificant result $P=0.468$ (Fig. 6.16, tables 6.1, 6.2, 6.3 and 6.4).

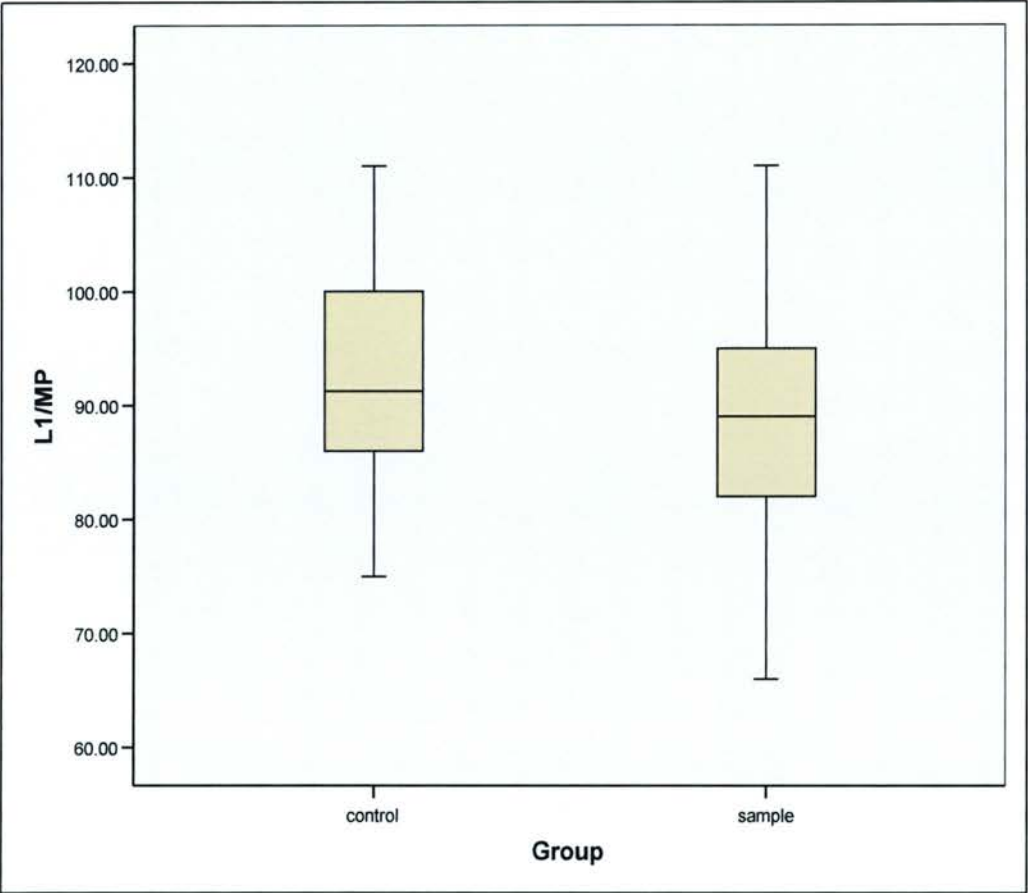
Figure 6.16 Upper incisor to the Maxillary (Nasal) Plane (U1/NL)



6.1.12 Lower Incisor to Mandibular Plane

L1/MP has been found to be *smaller* in the OSAHS group than the control, mean 88.71°, 92.50°, SD 9.10002 and 8.29459 respectively, but with statistically insignificant result $P=0.296$ (Fig. 6.17, tables 6.1, 6.2, 6.3 and 6.4).

Figure 6.17 Lower incisor to the Mandibular Plane (L1/MP)



6.2 LINEAR MEASUREMENTS (12 variables)

- Upper anterior facial height (N-NL)
- Lower anterior facial height (Gn-NL)
- Upper posterior facial height (S-NL)
- Lower posterior facial height (Go-NL)
- Anterior cranial base (S-N)
- Maxillary length (ANS-PNS)
- Mandibular length (Me-Go)
- Overbite (OB)
- Overjet (OJ)
- Hyoid bone position (H-H1)
- Hyoid bone position (H-H2)
- Hyoid bone position (H-H1) + (H-H2)

Table 6.5 Linear Measurements (Multivariate analysis)
Descriptive Statistics (B)

Group		Mean	Std. Deviation	N
N-NL	control	53.7333	2.67083	30
	sample	53.9462	4.11943	65
	Total	53.8789	3.71005	95
Gn-NL	control	62.6000	5.27421	30
	sample	68.3923	7.40011	65
	Total	66.5632	7.29334	95
S-NL	control	42.8667	3.55483	30
	sample	43.6000	3.79267	65
	Total	43.3684	3.71613	95
Go-NL	control	32.8833	5.09341	30
	sample	36.2000	5.97639	65
	Total	35.1526	5.89269	95
N-S	control	73.4333	3.31593	30
	sample	73.3462	4.05906	65
	Total	73.3737	3.82250	95
ANS-PNS	control	57.5833	3.36074	30
	sample	54.2615	4.99539	65
	Total	55.3105	4.78372	95
Me-Go	control	74.3833	5.69889	30
	sample	73.2077	6.55320	65
	Total	73.5789	6.28969	95
OB	control	3.4667	2.11291	30
	sample	3.9308	2.80885	65
	Total	3.7842	2.60692	95
OJ	control	3.4167	2.64602	30
	sample	3.3154	2.60494	65
	Total	3.3474	2.60429	95
H-H1	control	18.5833	4.72171	30
	sample	22.8769	6.50843	65
	Total	21.5211	6.30430	95
H-H2	control	8.6667	5.99904	30
	sample	12.2077	6.22614	65
	Total	11.0895	6.34302	95
(H-H1)+ (H-H2)	control	26.5833	9.02113	30
	sample	35.1000	11.67670	65
	Total	32.4105	11.56618	95

Table 6.6 Linear Measurements Correlation Statistics

	N-NL	Gn-NL	S-NL	Go-NL	N-S	ANS-PNS	Me-Go	OB	OJ	H-H1	H-H2
Gn-NL	0.296 0.004										
S-NL	0.188 0.069	0.404 0.000									
Go-NL	0.385 0.000	0.330 0.001	0.169 0.102								
N-S	0.433 0.000	0.474 0.000	0.309 0.002	0.507 0.000							
ANS-PNS	0.438 0.000	0.233 0.023	0.283 0.005	0.269 0.008	0.534 0.000						
Me-Go	0.383 0.000	0.270 0.008	0.276 0.007	0.273 0.007	0.595 0.000	0.502 0.000					
OB	-0.046 0.659	-0.193 0.061	-0.126 0.223	-0.178 0.084	-0.040 0.698	-0.186 0.072	-0.101 0.329				
OJ	0.121 0.245	0.045 0.662	0.169 0.102	-0.031 0.769	0.004 0.966	0.215 0.037	-0.043 0.682	0.360 0.000			
H-H1	0.189 0.066	0.213 0.038	0.179 0.082	0.081 0.433	0.112 0.281	0.014 0.891	0.023 0.823	0.129 0.213	0.065 0.535		
H-H2	0.282 0.006	0.267 0.009	0.230 0.025	0.307 0.003	0.239 0.020	0.286 0.005	0.192 0.062	0.091 0.378	0.090 0.387	0.723 0.000	
(H-H1) + (H-H2)	0.251 0.014	0.245 0.016	0.197 0.055	0.220 0.032	0.181 0.079	0.140 0.176	0.093 0.370	0.144 0.164	0.095 0.358	0.929 0.000	0.913 0.000
	N-NL	Gn-NL	S-NL	Go-NL	N-S	ANS-PNS	Me-Go	OB	OJ	H-H1	H-H2

Table 6.7 Linear Measurements, Multivariate Tests(c)

This simultaneously tests each factor effect (group) on the dependent variables. Wilks' Lambda is the usual test to quote when there are more than two dependent variables, although for each test the F-statistic is the same. Hence, there is a statistically significant difference between the sample and control patients ($p < 0.001$).

Effect	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared	Noncent. Parameter	Observed Power(a)
Intercept	Pillai's Trace	.998	3232.001(b)	12.000	.000	.998	38784.009	1.000
	Wilks' Lambda	.002	3232.001(b)	12.000	.000	.998	38784.009	1.000
	Hotelling's Trace	472.976	3232.001(b)	12.000	.000	.998	38784.009	1.000
	Roy's Largest Root	472.976	3232.001(b)	12.000	.000	.998	38784.009	1.000
Group	Pillai's Trace	.497	6.750(b)	12.000	.000	.497	80.996	1.000
	Wilks' Lambda	.503	6.750(b)	12.000	.000	.497	80.996	1.000
	Hotelling's Trace	.988	6.750(b)	12.000	.000	.497	80.996	1.000
	Roy's Largest Root	.988	6.750(b)	12.000	.000	.497	80.996	1.000

a Computed using alpha = .05
b Exact statistic
c Design: Intercept+Group

Table 6.8 Parameter Estimates

This allows you to assess the significance of the factor 'group' on each of the dependent variables. For example, for the variable N-NL, 'control' is not statistically significantly different from 'sample' (p=0.797). 'Sample' is set to be the reference category, which is why the coefficient (B) is set to 0.

Dependent Variable	Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared	Noncent. Parameter	Observed Power(a)
						Lower Bound	Upper Bound			
N-NL	Intercept	53.946	.462	116.646	.000	53.028	54.865	.993	116.646	1.000
	[Group=control]	-.213	.823	-.259	.797	-1.847	1.421	.001	.259	.058
	[Group=sample]	0(b)
Gn-NL	Intercept	68.392	.845	80.983	.000	66.715	70.069	.986	80.983	1.000
	[Group=control]	-5.792	1.503	-3.854	.000	-8.777	-2.808	.138	3.854	.968
	[Group=sample]	0(b)
S-NL	Intercept	43.600	.461	94.490	.000	42.684	44.516	.990	94.490	1.000
	[Group=control]	-.733	.821	-.893	.374	-2.364	.897	.009	.893	.143
	[Group=sample]	0(b)
Go-NL	Intercept	36.200	.709	51.062	.000	34.792	37.608	.966	51.062	1.000
	[Group=control]	-3.317	1.262	-2.629	.010	-5.822	-.811	.069	2.629	.739
	[Group=sample]	0(b)
N-S	Intercept	73.346	.477	153.882	.000	72.400	74.293	.996	153.882	1.000
	[Group=control]	.087	.848	.103	.918	-1.597	1.772	.000	.103	.051
	[Group=sample]	0(b)
ANS-PNS	Intercept	54.262	.564	96.166	.000	53.141	55.382	.990	96.166	1.000
	[Group=control]	3.322	1.004	3.308	.001	1.328	5.316	.105	3.308	.906
	[Group=sample]	0(b)
Me-Go	Intercept	73.208	.781	93.697	.000	71.656	74.759	.990	93.697	1.000
	[Group=control]	1.176	1.390	.846	.400	-1.585	3.937	.008	.846	.133
	[Group=sample]	0(b)

Continued Table 6.8 Parameter Estimates

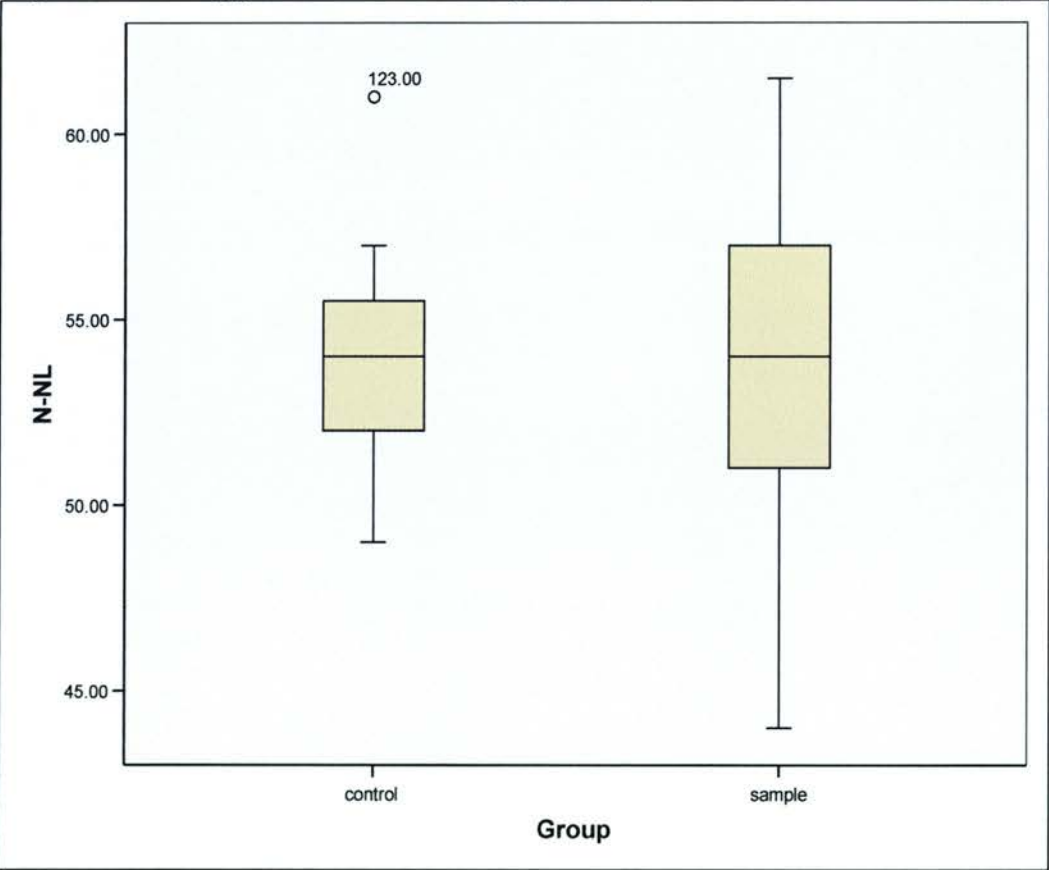
Dependent Variable	Parameter	B	Std. Error	t	Sig.	95% Confidence Interval		Partial Eta Squared	Noncent. Parameter	Observed Power(a)
						Lower Bound	Upper Bound			
OB	Intercept	3.931	.324	12.134	.000	3.287	4.574	.613	12.134	1.000
	[Group=control]	-.464	.576	-.805	.423	-1.609	.681	.007	.805	.125
	[Group=sample]	0(b)
OJ	Intercept	3.315	.325	10.211	.000	2.671	3.960	.529	10.211	1.000
	[Group=control]	.101	.578	.175	.861	-1.046	1.249	.000	.175	.053
	[Group=sample]	0(b)
H-H1	Intercept	22.877	.745	30.696	.000	21.397	24.357	.910	30.696	1.000
	[Group=control]	-4.294	1.326	-3.237	.002	-6.927	-1.660	.101	3.237	.893
	[Group=sample]	0(b)
H-H2	Intercept	12.208	.764	15.987	.000	10.691	13.724	.733	15.987	1.000
	[Group=control]	-3.541	1.359	-2.606	.011	-6.239	-.843	.068	2.606	.732
	[Group=sample]	0(b)
(H-H1)+ (H-H2)	Intercept	35.100	1.354	25.919	.000	32.411	37.789	.878	25.919	1.000
	[Group=control]	-8.517	2.410	-3.534	.001	-13.302	-3.731	.118	3.534	.938
	[Group=sample]	0(b)

a Computed using alpha = .05
b This parameter is set to zero because it is redundant

6.2.1 Upper Anterior Facial Height

N-NL has appeared *longer* in the OSAHS group than the control, mean 53.95mm, 53.73mm, SD 4.11943 and 2.67083 respectively. It shows insignificant result $P=0.797$ (Fig. 6.18, tables 6.5, 6.6, 6.7 and 6.8).

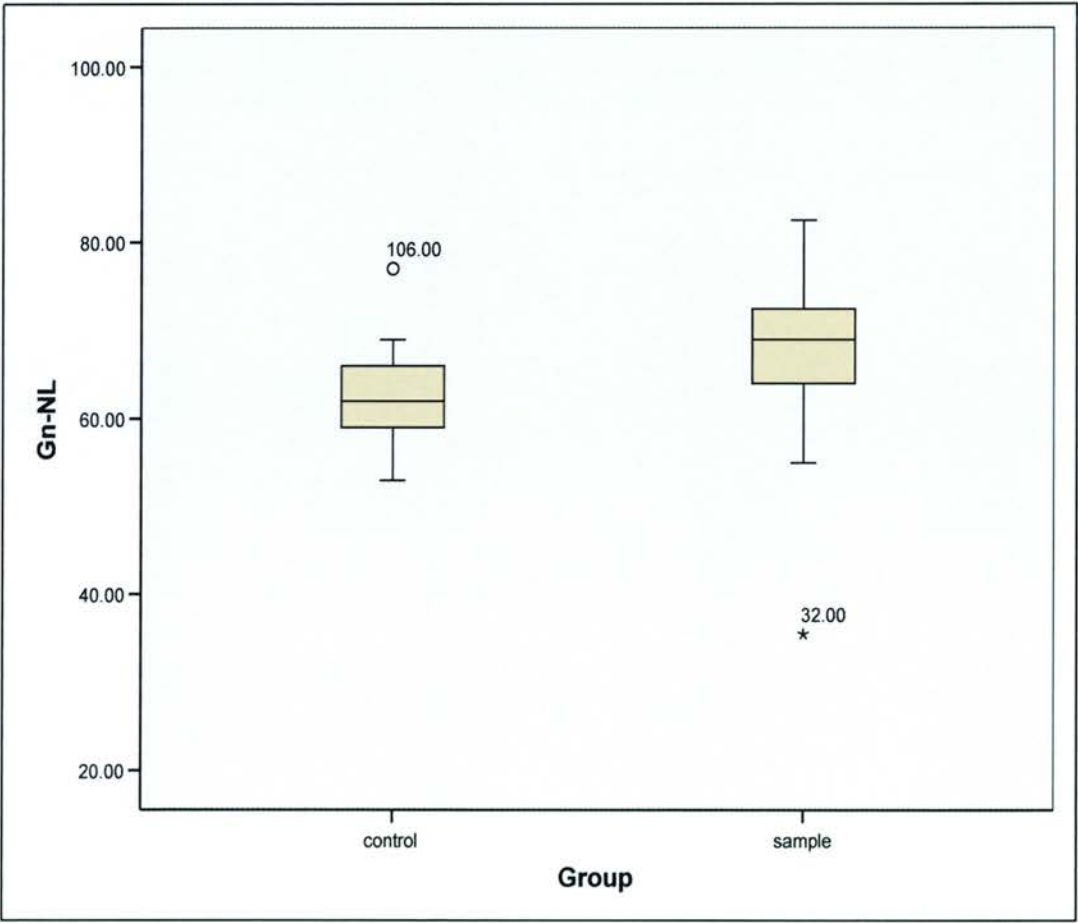
Figure 6.18 Upper anterior facial height (N-NL)



6.2.2 Lower Anterior Facial Height

Gn-NL has shown to be *longer* in the OSAHS than the control group, mean 68.39mm, 62.60mm, SD 7.40011 and 5.27421 respectively. It shows highly significant result $P=0.000***$ (Fig. 6.19, tables 6.5, 6.6, 6.7 and 6.8).

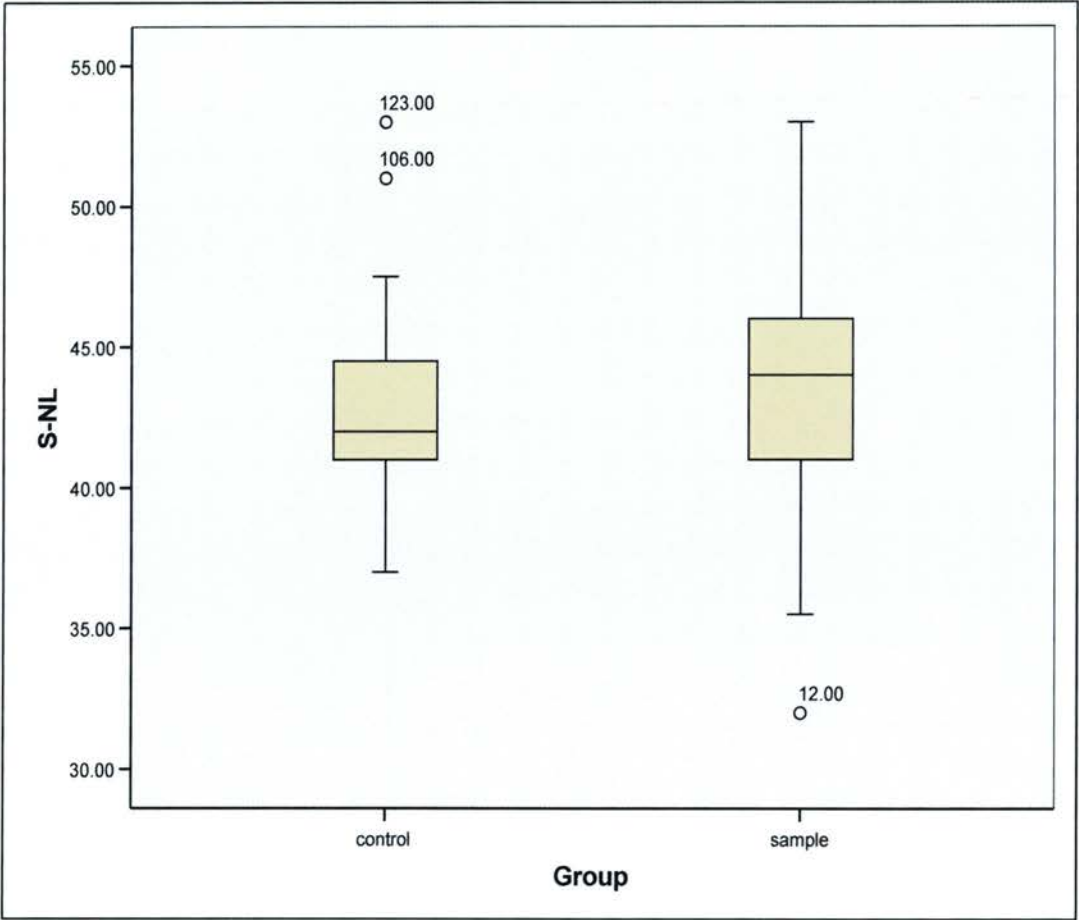
Figure 6.19 Lower anterior facial height (Gn-NL)



6.2.3 Upper Posterior Facial Height

S-NL has found to be *increased* in the OSAHS group when compared to the control, mean 43.60mm, 42.87mm, SD 3.79267 and 3.55483 respectively, but it is statistically insignificant $P=0.374$ (Fig. 6.20, tables 6.5, 6.6, 6.7 and 6.8).

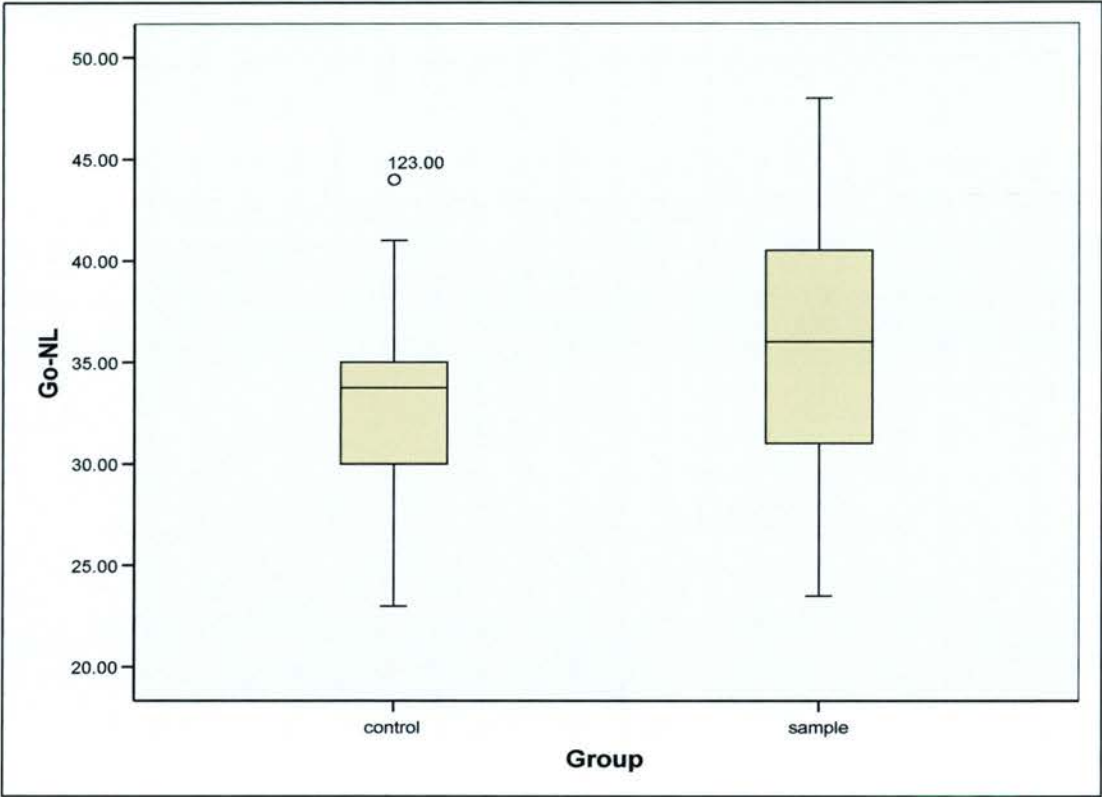
Figure 6.20 Upper posterior facial height (S-NL)



6.2.4 Lower Posterior Facial Height

Go-NL has shown to be *longer* in the OSAHS than the control, mean 36.20mm, 32.88mm, SD 5.97639 and 5.09341 respectively. Statistically, it is highly significant $P=0.010^*$ (Fig. 6.21, tables 6.5, 6.6, 6.7 and 6.8).

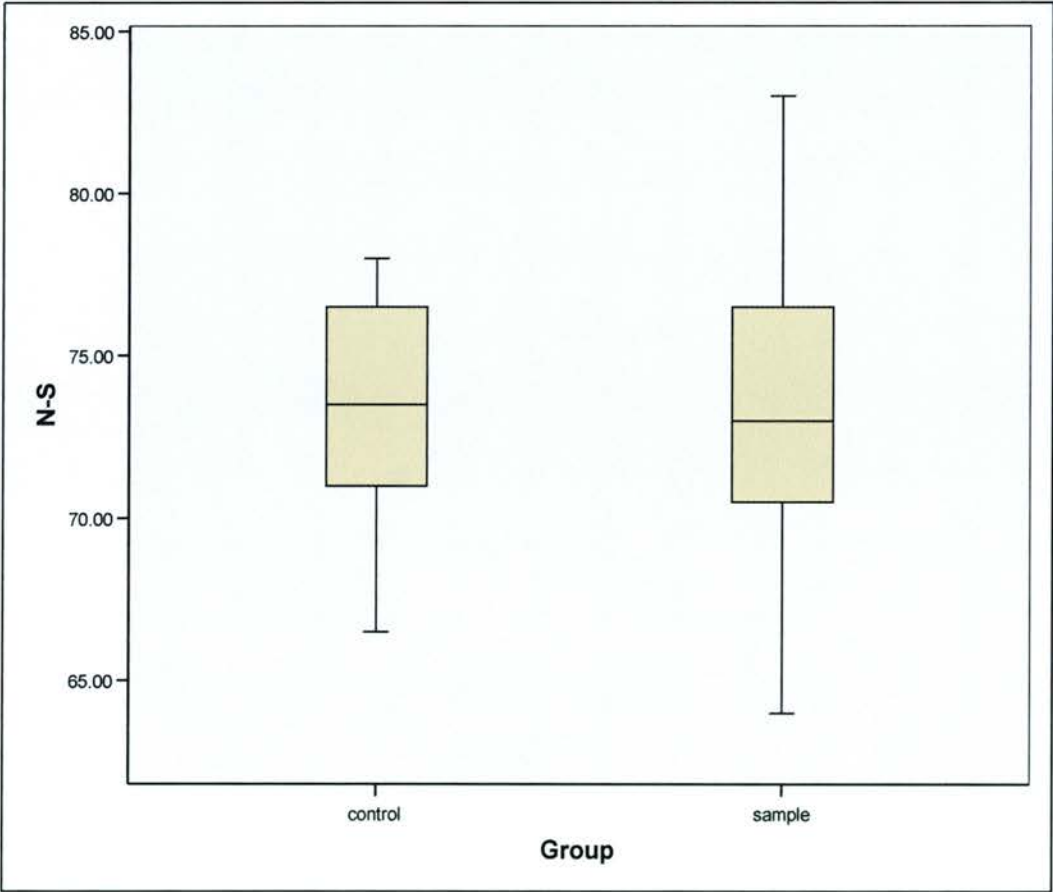
Figure 6.21 Lower posterior facial height (Go-NL)



6.2.5 Anterior Cranial Base Length

N-S length has appeared to be *shorter* in the OSAHS than in the control group, mean 73.35mm, 73.43mm, SD 4.05906 and 3.31593 respectively. They are highly correlated, but statistically insignificant $P=0.918$ (Fig. 6.22, tables 6.5, 6.6, 6.7 and 6.8).

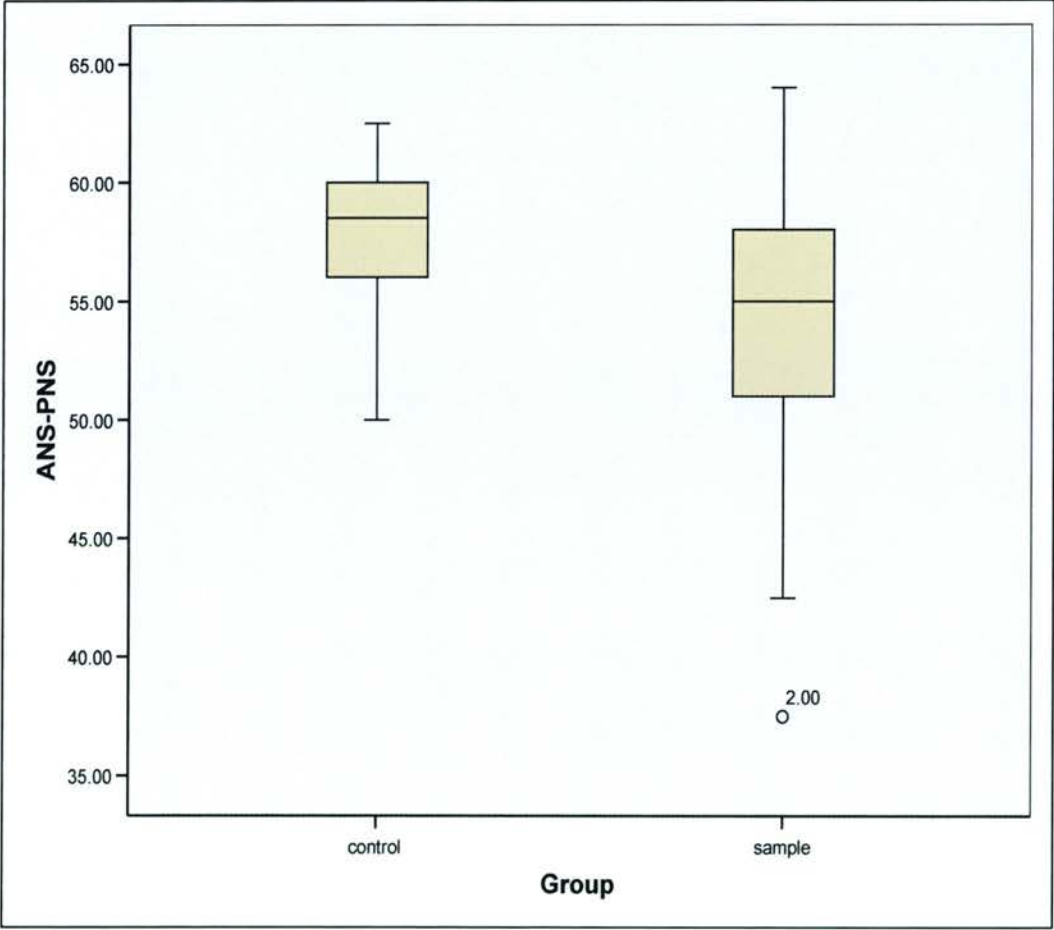
Figure 6.22 Anterior cranial base (N-S)



6.2.6 Maxillary Length

ANS-PNS has shown to be *shorter* in the OSAHS group than the control, mean 54.26mm and 57.58mm, SD 4.05906 and 3.31593 respectively, and a highly significant result $P=0.000***$ (Fig. 6.23, tables 6.5, 6.6, 6.7 and 6.8).

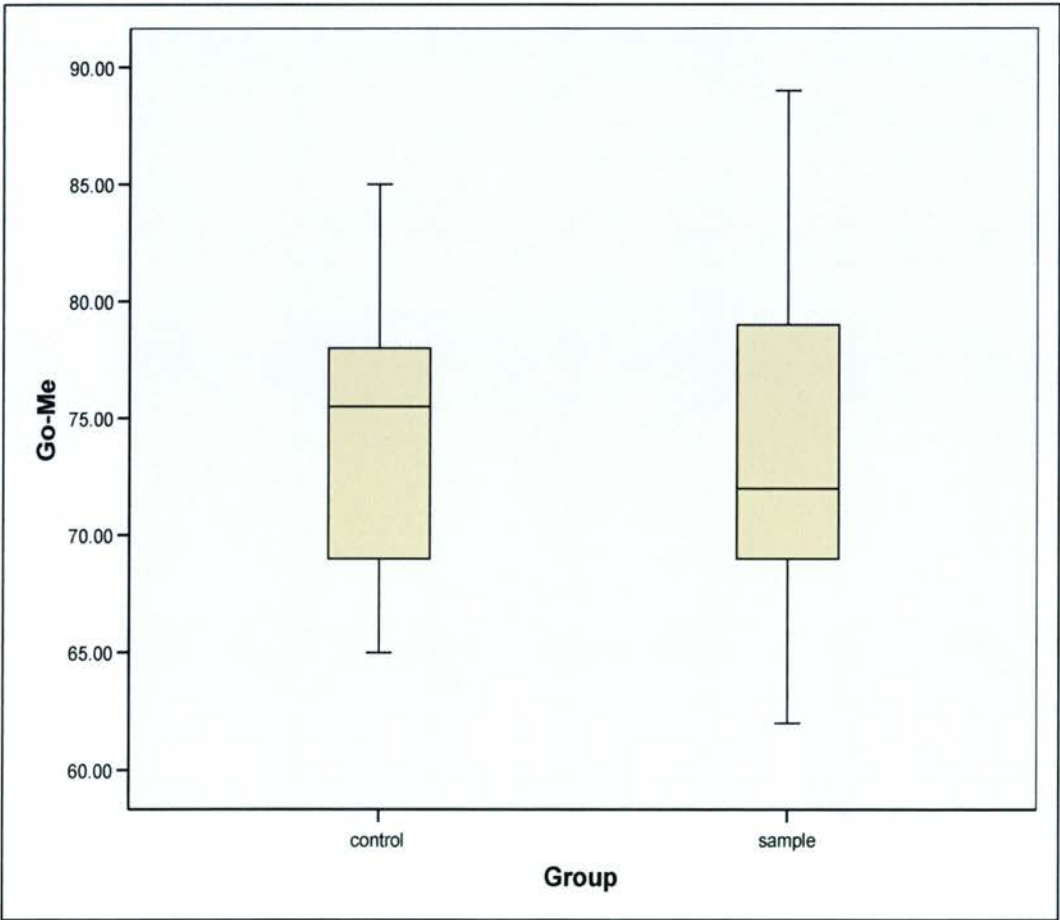
Figure 6.23 Maxillary length (ANS-PNS)



6.2.7 Mandibular Length

Mandibular plane (Me-Go) has appeared *shorter* in the OSAHS group than the control, mean 73.21mm, 74.38mm, SD 6.55320 and 5.69889 respectively, and with a high statistical significance $P=0.002^{**}$ (Fig. 6.24, tables 6.5, 6.6, 6.7 and 6.8).

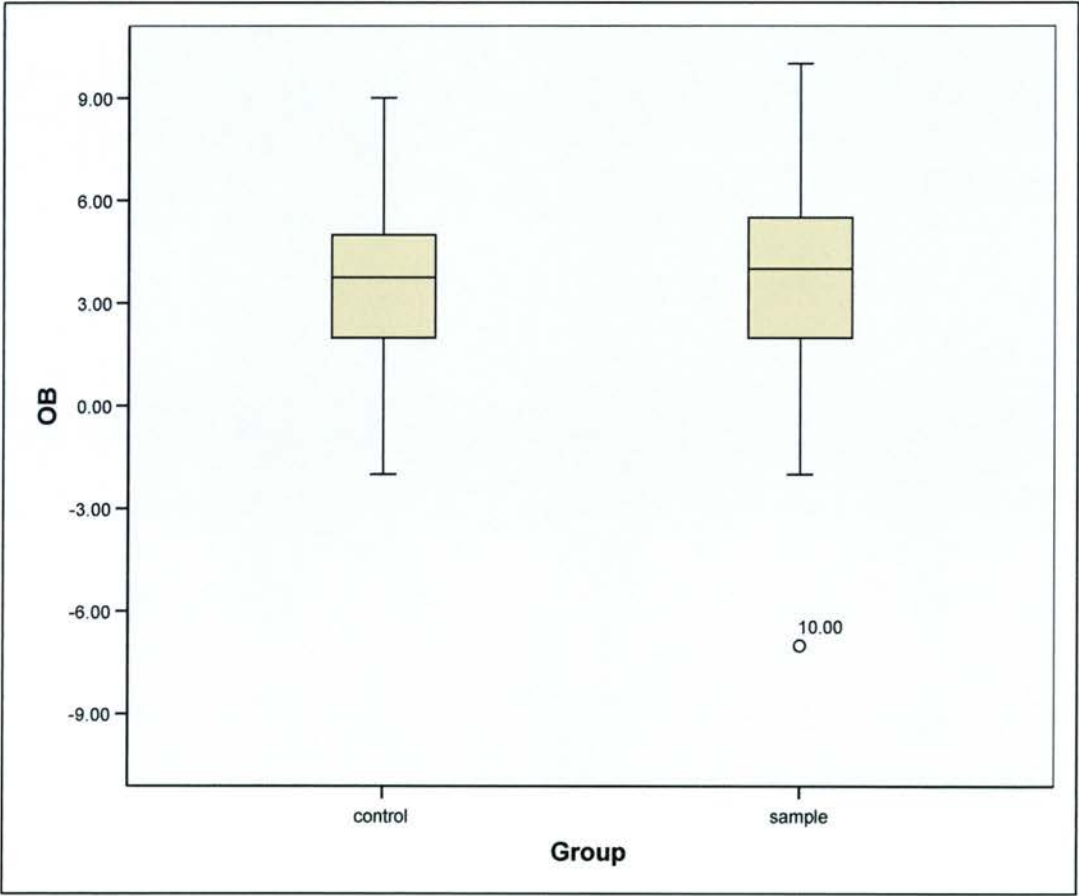
Figure 6.24 Mandibular length (Me-Go)



6.2.8 Overbite

Overbite has shown to be *deeper* in the OSAHS group than the control, mean 3.93mm, 3.47mm, SD 2.80885, 2.11291 respectively, but statistically insignificant $P=0.318$ (Fig. 6.25, tables 6.5, 6.6, 6.7 and 6.8).

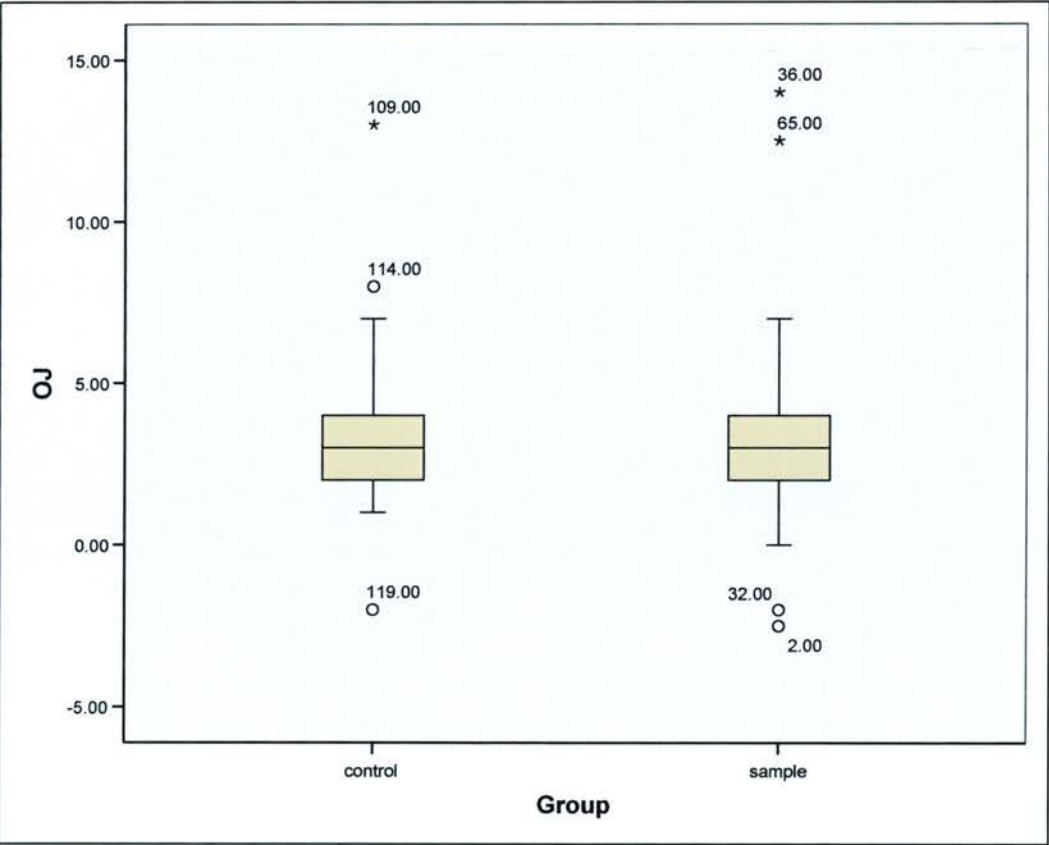
Figure 6.25 **Overbite**



6.2.9 Overjet

Overjet has shown to be *reduced* in the OSAHS group than the control, mean 3.32mm, 3.42, SD 2.60494 and 2.64602 respectively, but statistically insignificant $P=0.729$ (Fig. 6.26, tables 6.5, 6.6, 6.7 and 6.8).

Figure 6.26 **Overjet**

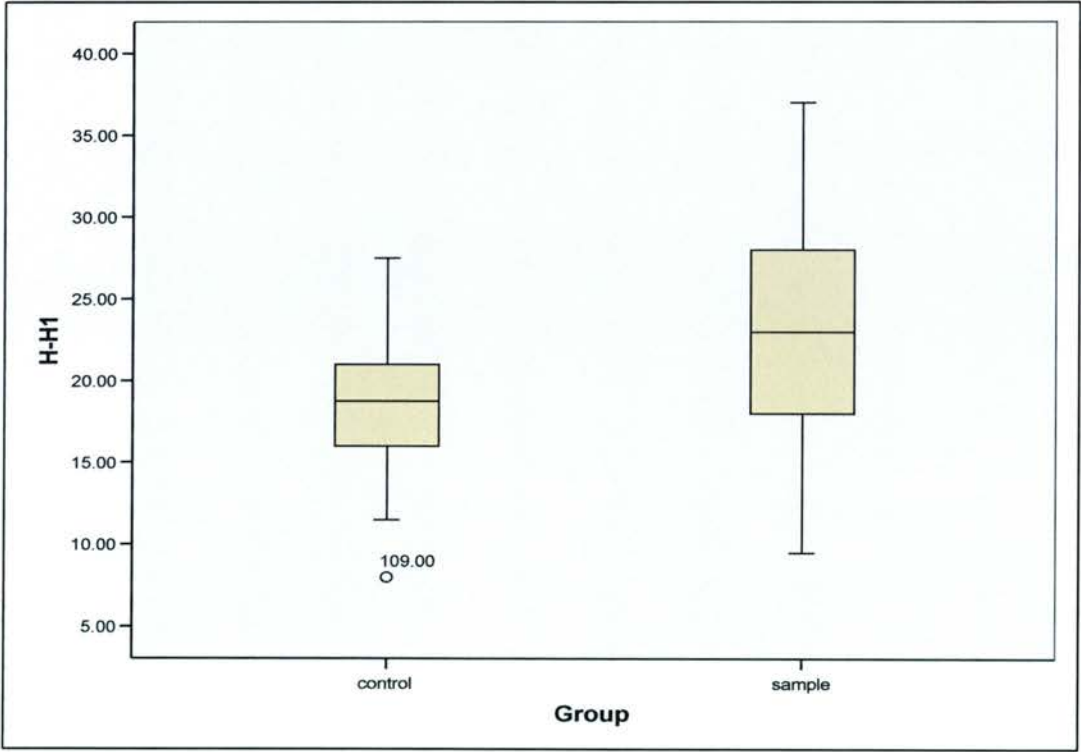


6.2.10 Hyoid Bone Position

6.2.10.1 Hyoid Bone Position (H-H1)

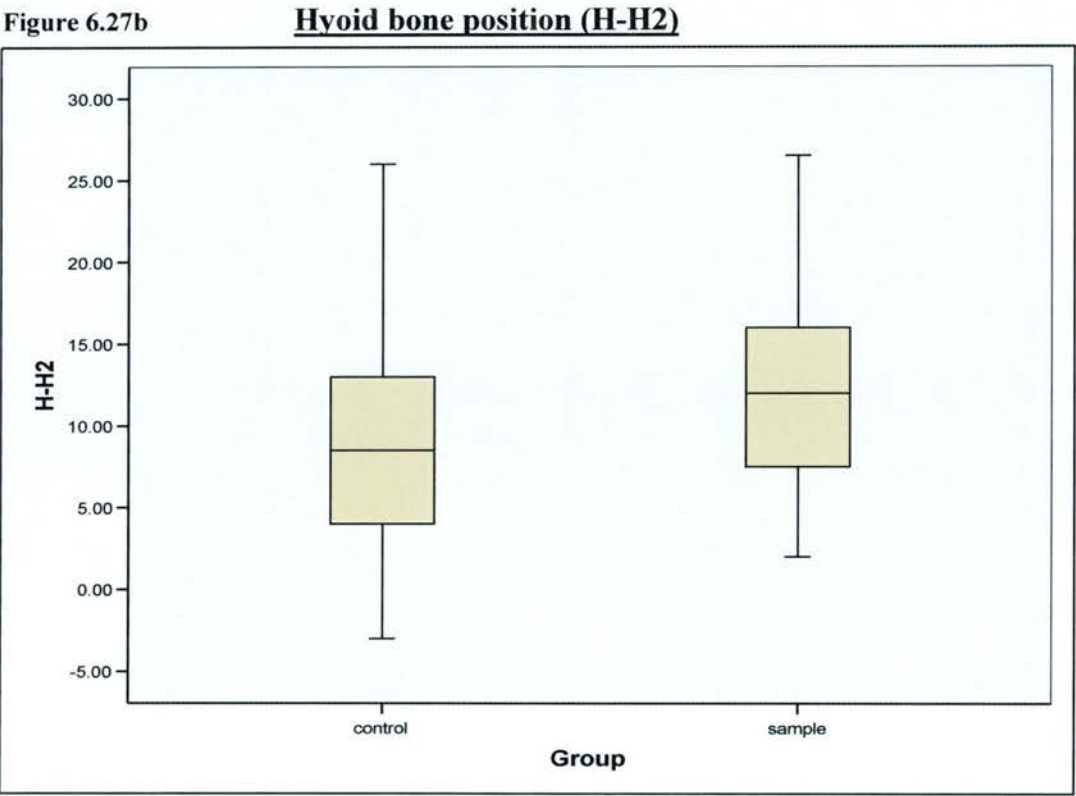
Hyoid bone has been found to be more *inferiorly* positioned in the OSAHS subjects than the control, mean 22.88mm, 18.58, SD 6.50843 and 4.72171 respectively, with high statistical significance $P=0.002^{**}$ (Fig. 6.27a, tables 6.5, 6.6, 6.7 and 6.8).

Figure 6.27a Hyoid bone position (H-H1)



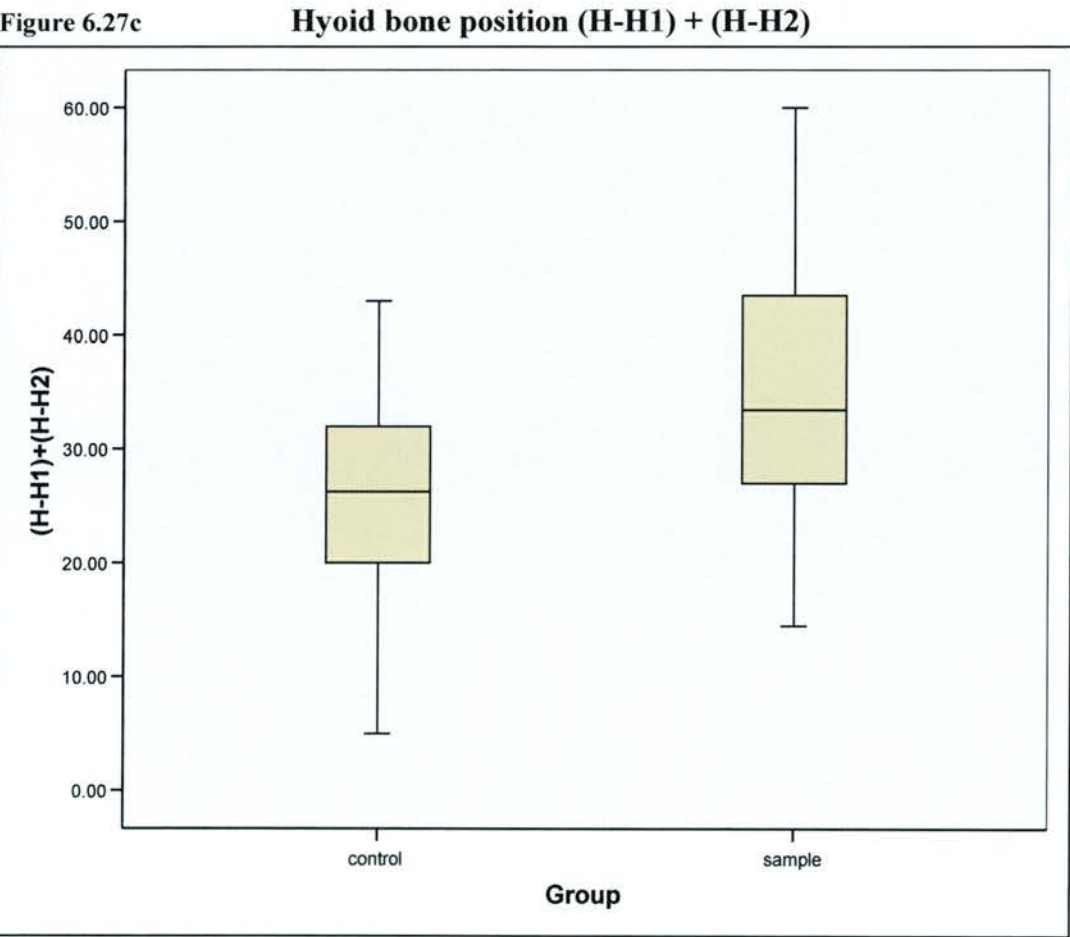
6.2.10.2 Hyoid Bone Position (H-H2)

H-H2 also appeared to be inferiorly positioned in the OSAHS than the control, mean 12.21mm, 8.67mm, SD 6.22614 and 5.99904 respectively with high significant result $P=.011$ (Fig. 6.27b, tables 6.5, 6.6, 6.7 and 6.8).



6.2.10.3 Hyoid Bone Position (H-H1) + (H-H2)

(H-H1) + (H-H2) is inferiorly positioned in the OSAHS subjects than the control, mean 35.10mm, 26.58mm, SD 11.67670 and 9.02113 respectively, and a high significant result $P=.001^{**}$ (Fig. 6.27c, tables 6.5, 6.6, 6.7 and 6.8).



DISCUSSION

Cephalometric radiography has a long tradition as a diagnostic and follow-up technique in the study of cranio-facial morphology (Broadbent, 1931) and in the surgical management of cranio-facial deformities (Burstone et al., 1978).

Availability of normative data and the possibility of superimposition of long-term serial records have given this method a unique position (Burstone et al., 1975; Behrents 1985a and 1985b).

Recently, several reports regarding the deviated cephalometric data of OSAHS patients have been published with some controversies (Maltais et al., 1991; Davies and Straddling, 1990 and 1991). Consequently, a comprehensive study of the subject to solve some of these controversies is needed.

The characteristic appearance of the typical patient severely affected by obstructive sleep apnoea / hypopnoea syndrome led Osler (1901) to characterize this condition as 'Pickwickian' according to the novel by Charles Dickens (1836) in which such a condition was described. Subsequently the term 'Pickwick syndrome' has sometimes been used for OSAHS. Although no formal description of the head posture in this condition has been made, an extended head posture is generally recognized by clinicians as being a characteristic feature of the appearance of patients with obstructive sleep apnoea (Cote, 1988).

In the field of Orthodontics, the natural head posture is of interest from two aspects:

1. In the diagnostic assessment of facial aesthetics in orthodontic and orthognathic surgery treatment plan.
2. In the assessment of the role of head posture in postnatal facial morphogenesis.

In assessment of facial aesthetics, emphasis is laid on the posture of the head in relation to a gravity-determined true vertical.

Several cephalometric analyses have been developed for the purpose of performing such aesthetic assessments of the maxillary and mandibular protrusion in relation to a gravity-determined true vertical (Moorees et al., 1976; Cooke and Wei, 1988; Lundstrom and Lundstrom, 1989).

Angular Measurement

It may be noted, however, that widely differing means of the cranio-cervical angulation have been reported by different authors. A survey by Solow and Tallegran (1971a) of means for NSL/VER in five different studies showed a range from 89.6° to 102.4°. This can be taken to indicate that the cranio-vertical angle is particularly very sensitive to differences in methodology for recording of head posture.

Assessment of facial protrusion in relation to a gravity-determined vertical thus would seem to require further standardization of the positioning procedures used in such studies.

The role of head posture in facial development has been demonstrated in a series of studies which provide for the existence of a sequence of events comprising:

1. Obstruction of the upper airways;
2. Increase in the cranio-cervical angulation;
3. Vertical direction of the facial development.

It is important to notice, however, that the posture involved in this sequence of events is the position of the head in relation to the cervical column. Changes in this angle are mediated by changes in the cranio-vertical and in the cervico-horizontal angles. An increase in cranio-cervical angulation thus can be mediated by an extension of the head in relation to the true vertical, by a forward inclination of the cervical column or by a combination of both.

An increase in the cranio-cervical angle can be triggered by various types of obstruction of the upper airway. One reason for this physiological mechanism could be that such a change in posture will increase the diameter of the airway and thus reduce the airway resistance. Another reason could be that, observed by Ricketts (1968), an increase in the cranio-cervical angle will lift the head away from the hyo-mandibular complex and thus, facilitate the transition from nasal breathing to mouth breathing which occurs in many subjects with a larger upper airway resistance caused by nasal or naso-pharyngeal obstruction.

Studies of head posture in subjects with adenoidal obstruction have demonstrated an average increase in cranio-cervical angulation of about 2° (Solow B and Greve E, 1979; Woodside D and Linder-Aronson S, 1979). This increase is mediated by an increase in the cranio-vertical relationship, whereas the average cervical inclination is not affected. After adenoidectomy this extended head posture in the

obstructed children has shown to normalize. Thus, in individual children a reduction of the cranio-cervical angle of up to 9° has been found (Solow B and Greve E, 1979).

It has long been known that various kind of craniofacial anomalies are closely related to upper airway obstruction which may lead to the OSAHS condition. Craniosynostosis syndrome such as Crouzon or Apert (Schafer ME, 1982), Pierre Robin syndrome (Lapidot A and Ben-Hur N, 1975), and Treacher Collins syndrome (Johnston et al., 1981) were among these.

This present study provides further evidence for the suggestion that obstruction of the upper airway may trigger an increase in the cranio-cervical angulation. Six cranio-cervical angles were statistically different in the OSAHS group when compared to the control with special significance to the angles formed with the OPT. The large difference in cranio-cervical angulation was mediated by a forward inclination of the cervical column. A physiological requirement for a major increase in cranio-cervical angulation due to airway obstruction therefore can only be met by a forward inclination of the cervical column.

A similar mechanism, in head tilting mediates minor changes in head posture whereas larger changes are mediated by changes in cervical inclination, was observed in a study of how subjects produced the change in head posture from the self-balance position to the mirror position (Solow B and Tallegran A, 1971b).

The angle of the cervical curvature (OPT/CVT) has shown to be reduced in the OSAHS group (mean 6.46°, SD 3.17), when compared to the control (mean 10.6°, SD 4.42). This further shows forward positioning of the head. Solow et al. (1993)

also found this angle to be lesser in the OSAHS group mean 4.5° and SD 2.91. Tangugsorn et al., (1995) got a different result, increased (OPT/CVT) angle in the OSAHS (100 patients, mean 3.55° , SD 2.96) than the control (36 patients, mean 1.08° , SD 2.96). Sakakibara et al., (1999) found (OPT/CVT) to be also reduced in the obese OSAHS group (mean 1.1° , SD 2.6), than the control (mean 1.5° , SD 3.1), and they have also found this angle to be more reduced in the non-obese OSAHS group (0.9° , SD 1.9).

The angle of maxillary inclination (NL/NSL) or the angle describing the vertical dimension of the upper face showed about the same values in patients and control (Lyberg et al., 1989), whereas in this present study appeared to have been lesser in the OSAHS group (mean 8.41° , SD 3.60) when compared to the control, (mean 8.8° , SD 2.42), which indicates a downward and forward rotation of the cranio-maxillary complex, and a shorter upper face.

Lyberg et al., (1989) found the angle describing the vertical dimension of the lower face (MP/NSL) was significantly greater ($P<0.05$) in the patients, indicating more cranial positioning of the gonial angle. Our study showed the angle of mandibular inclination (MP/NSL) appeared to be minimally reduced when comparing the OSAHS group (mean 36.20° , SD 6.19) with the control group (mean 36.35° , 6.43), which explain the downward and backward rotation of the mandible and more caudally positioning of the gonial angle which could be due to increase in ramus length.

This present study showed the inter-maxillary angle (NL/MP) to be increased in the OSAHS group (mean 28.34°, SD 6.24) when compared to the control, (mean 26.72°, SD 6.77), this confirm the downward and forward rotation of the maxilla and downward and backward rotation of the mandible. Battagel and L'Estrange (1996) found the maxillary mandibular plane angle to be increased in the OSAHS group than the control, mean 26.5° and 24.2° respectively. Tangugsorn et al., (1995) also found the (NL/MP) angle to be increased in the OSAHS (mean 2.78°), when compared to the control (mean 2.11°).

A slight depression of the sphenoidal complex in the clivus region was observed, when considering (FH/NSL) angle which was increased in the OSAHS group mean 8.25°, SD 3.17 when compared to control mean 8.10°, SD 3.92 (Tangugsorn et al., 1995). This present study found (FH/NSL) to be similar to those of Tangugsorn et al., (1995), with a mean higher in the OSAHS group than that of the control, 9.35° and 8.10° respectively. When the (FH/NSL) angle was taken into consideration, the whole structure of the cranial base was rotated slightly counter-clockwise in the sagittal plane in the OSAHS group; this was worsened by the retrognathic position of the maxilla and the mandible, (Tangugsorn et al., 1995).

Battagel and L'Estrange (1996) found that the (SNA) to be increased in the OSAHS group when compared to the control, mean 81.6° and 80.6° respectively. Tangugsorn et al., found the SNA to be smaller in the OSAHS (mean 80.34°) than the control group 81.79°. Sakakibara et al., (1999) found SNA to be increased in the obese OSAHS group (mean 83.7°, SD 4.0) than the control (mean 82.5°, SD

4.3), but reduced in the non-obese OSAHS group (82.1°, SD 4.6). Our data in relation to (SNA) proved to be increased in OSAHS group (mean 82.31°, SD 6.46) than the control group (mean 76.25°, SD 18.99) with a difference of 6.06° which is similar to the results of Battagel and L'Estrange (1996).

Battagel and L'Estrange, (1996) found that (SNB) was increased in the OSAHS group than the control, mean 79.2° and 78.6° respectively, while Tangugsorn et al., (1995) found SNB to be smaller in the OSAHS group (mean 77.56°) when compared to the control group (mean 79.69°). Sakakibara et al., (1999) found SNB to be increased in the obese OSAHS group (mean 79.2°, SD 4.1) than the control (mean 78.8°, SD 3.4) but reduced in the non-obese OSAHS group (mean 77.7°, SD 4.6). A smaller (SNB) angle has long been used to indicate mandibular retrusion relative to Nasion (Riley et al., 1983; Jamieson et al., 1986; Hochban and Brandenburg, 1994). Obviously, factors other than mandibular retrusion should be well controlled when explaining the significance of a decreased (SNB) angle.

This present study showed (SNB) to be increased in the OSAHS group (mean 79.1°, SD 8.09) when compared to the control (mean 76.9°, SD 3.71) respectively, with a difference of 2.2°. This explains that the retrognathic position of the mandible in the OSAHS group was less than the control which indicates clockwise rotation of the mandible, which is clearly due to the concomitant shortening of the cranial base in the OSAHS patients.

Battagel and L'Estrange (1996) found the (ANB) angle to be increased in the OSAHS group than the control, mean 2.1°, 1.9° respectively. Tangugsorn et al.,

(1995) also found ANB angle increased in the OSAHS group mean (2.78°), when compared to the control mean 2.11° . Sakakibara et al., (1999) found this angle to be increased in the obese OSAHS group (mean 4.6° , SD 2.7) and also increased in the non-obese OSAHS group (mean 4.5° , SD 2.7) than the control (mean 3.6° , SD 2.7).

The present study showed minimal increase of the (ANB) angle in the OSAHS group (mean 4.16° , SD 3.78), when compared to the control, (mean 4.03° , SD 3.70) with a difference of 0.13° . This indicates a more skeletal class II cases than the skeletal class III cases among the OSAHS group.

Battagel JM and L'Estrange PR (1996), found the upper incisors to maxillary plane (U1/NL) mean 108.9° to be reduced in the OSAHS than the control mean 110° , and the lower incisors to mandibular plane (L1/MP) mean 90.9° , to be increased in the OSAHS than the control mean 89.1° .

This present study showed that the upper incisors to maxillary plane angle U1/NL (mean 106.46° , SD 7.90) and the lower incisors to mandibular plane angle L1/MP (mean 88.71° , SD 9.06) to be reduced in the OSAHS group, than the control U1/NL (mean 107.80° , SD 9.17), L1/MP (mean 92.50° , SD 9.10). The results in our study showed to be similar to that by Battagel and L'Estrange in relation to (U1/NL), and different to the same study in relation to (L1/MP), this could be due to the severity of the OSAHS condition in our group and also could be due to proclination of the lower incisors in the control.

Our data showed the inter incisal angle (U1/L1) to be increased in the OSAHS group (mean 136.77° , SD 14.01) than the control (mean 132.15° , SD 12.08),

which confirms the reduced angles of U1/NL and L1/MP. Dental relationship explains the downward and forward rotation of the maxilla and downward and backward rotation of the mandible.

Linear Measurement

Lyberg et al., (1989) found the upper anterior facial height (N-NL) to be increased in the OSAHS group (mean 56.4mm, SD 3.0) than the control (mean 54.7mm, SD 3.1), whereas Battagel JM and L'Estrange PR (1996) found the (N-NL) to be decreased in the OSAHS group (mean 52.7mm, SD 3.3) than the control (mean 54.4mm, SD 3.3). Tangugsorn et al., (1995) found the upper anterior facial height to be reduced in the OSAHS group (100 patients, 55.97mm, SD 3.39) when compared to the control (36 controls, mean 57.07mm, SD 3.53). This present study found (N-NL) to be similar to that of Lyberg et al., (1989), increased in the OSAHS group (65 subjects, mean 53.95mm, SD 4.12), than the control (30 controls, mean 53.73mm, SD 2.67), which indicates inferiorly positioned Nasion.

Lyberg et al., (1989) found increased lower anterior facial height (Gn-NL) in the OSAHS group (mean 73.4mm, SD 5.1) when compared to the control (mean 70.9mm, SD 5.5). Battagel JM and L'Estrange PR (1996) found reduced lower anterior facial height in the OSAHS group (mean 67.6mm, SD 7.2) when compared to the control (mean 69.2mm, SD 5.5). Tangugsorn et al., (1995) found the lower anterior facial height to be increased in the OSAHS group (mean 75.93mm, SD 6.34) than the control (mean 72.22mm, SD 4.70).

This present study showed an increase in the lower anterior facial height in the OSAHS group (mean 68.39mm, SD 7.40) when compared to the control (mean 62.60mm, SD 5.27) similar to that of Lyberg et al., (1989) and Tangugsorn et al., (1995) which is highly significant.

Lyberg et al., (1989) found the upper posterior facial height (S-NL) to be increased in the patients (25 patients, mean 45.2mm, SD 3.2) when compared to the control (10 controls, mean 44.0mm, SD 2.9). Tangugsorn et al., (1995) found that the S-NL to be reduced in the OSAHS group (mean 43.91mm, SD 3.34) when compared to the control (mean 45.25mm, SD 2.99).

This present study report similar results to the work of Lyberg et al (1989), increased upper posterior facial height in the OSAHS group (mean 43.60mm, SD 3.79) when compared to the control (mean 42.87mm, SD 3.55) but statistically insignificant.

Tangugsorn et al., (1995) found the lower posterior facial height to be reduced in the OSAHS group (mean 41.37mm, SD 5.99) when compared to the control (mean 43.32mm, SD 3.89). Lyberg et al., (1989) also found (Go-NL) to be reduced in the OSAHS group (mean 41.8mm, SD 5.9) when compared to the control (mean 42.6mm, SD 3.4). Our data were different from the above studies, it appeared increased in the OSAHS group (mean 36.20mm, SD 5.98) than the control (mean 32.88mm, SD 5.09), which indicate a clockwise rotation of the maxilla and a more caudally placed gonial angle which could be due to increase in ramus length.

The present study reported shorter anterior cranial base length (S-N) in the OSAHS group (mean 73.35mm, SD 4.06) when compared to the control (mean 73.43mm, SD 3.32). Tangugson et al., (1995) found the S-N to be shortened in the OSAHS group (mean 71.18mm, SD 3.3) than the control (mean 74.23mm, SD 3.16). The same findings also reported by Battagel JM and L'Estrange PR (1996), OSAHS (mean 70.0mm, SD 2.6) and the control (mean 72.4mm, SD 3.0). Sakakibara et al., (1999) found also shortened (S-N) in the OSAHS group (mean 71.9mm, SD 3.8) than the control (mean 73.5mm, SD 3.4). A recent study by Randall et al., (2000) in an age group 7-14 years found the (S-N) also to be shortened in the OSAHS group than the control. The fact that snorers had shortened cranial base (S-N) and maxilla (ANS-PNS) may suggest a narrowing in the sagittal dimension (Randall et al., 2000).

This present study showed maxillary length (ANS-PNS) to be shorter in the OSAHS group (mean 54.26mm, SD 5.00) when compared to the control (mean 57.58mm, SD 3.36), which is statistically highly significant $P=.001$, and confirm the decreased antero-posterior facial distance at (ANS-PNS). Lyberg et al., (1989) found the maxilla to be shorter in the OSAHS group (mean 55.7mm, SD 3.1) than the control (mean 56.8mm, SD 1.9). Tangugsorn et al., (1995) found the maxilla to be shortened in the OSAHS group (mean 54.86mm, SD 3.54) when compared to the control (mean 56.98mm, SD 3.89). More recently Sakakibara et al., (1999) found the ANS-PNS distance to be reduced in the obese OSAHS group (mean 52.6mm, SD 5.0), and more reduced in the non-obese OSAHS group (mean 51.5mm, SD 5.1) when compared to the control (mean 54.5mm, SD 4.4).

One of the most widely published deviating cephalometric data in OSAHS patients is the size and position of the mandible. Mandibular micrognathia and retrognathia has been frequently described (Valero A and Alroy G, 1965; Tammeling et al., 1972; Coccagna et al., 1978). Lyberg et al., (1989) found mandibular length to be shortened in the OSAHS group (mean 77.0mm, SD 5.2) when compared to the control (mean 78.2mm, SD 2.5). Tangugsorn et al., (1995) found also mandibular length to be shorter (Go-Gn) in the OSAHS group (mean 72.85mm, SD 5.09) than the control (mean 74.65mm, SD 5.29). The same result also found by Battagel JM and L'Estrange PR (1996) with a (mean 69.7mm, SD 5.7) in the OSAHS group and a (mean 72.8mm, SD 5.5) in the control group. More recently Sakakibara et al., (1999) found the mandibular length (Me-Go) distance to be reduced in the obese OSAHS group (mean 75.0mm, SD 5.6), and more reduced in the non-obese OSAHS group (mean 73.3mm, SD 5.3) when compared to the control (mean 77.0mm, SD 5.5). Our data found the mandibular length shorter in the OSAHS group (mean 73.21 mm, SD 6.55) when compared to the control (mean 74.38mm, SD 5.70), same results of previous studies. Bear SE and Priest JH, (1980) described a case of OSAHS and a class II malocclusion with retrognathic mandible. Bilateral osteotomies on the horizontal part of the mandible with interposition of iliac bone grafts after advancement of the mandible resulted in normalization of sleep patterns and amelioration of symptoms like snoring and excessive daytime sleepiness. Riley et al., (1984) described a surgical procedure combining advancement of an inferior mandible/chin fragment with anterior suspension of the hyoid. In essence, the effect of all these procedures is an anterior repositioning of the tongue and enlargement of the posterior airway space (PAS), i.e. the space between the base

of the tongue and posterior pharyngeal wall. In contrast, setback of the mandible for correction of mandibular prognathism can precipitate OSAHS (Guilleminault et al., 1985). In a recent study of habitually snoring and apnoeic children, reposition of the mandible was not essential to the development of upper-airway obstruction, but rather contributed by posterior crossbite caused by a reduced growth of the maxilla after continuous oral breathing, and anterior open-bite with lip incompetence, owing to a forward tongue position (Zucconi et al., 1999). Studies in adults have also demonstrated a significant reduction in the sagittal dimension of the anterior cranial base in apnoeic patients (Bacon et al., 1990), a reduction in cranial base and mandible in snorers, and a shorter maxilla in apnoeic patients (Zucconi et al., 1993). These studies suggest that habitual snorers might have an anatomic predisposition to airway obstruction. On the contrary, there are reports which indicate that cephalograms of OSAHS patients and those of simple snorers do not differ from one another (El-Sheikh et al., 1996; Andersson et al., 1991).

Tangugsorn et al., (1995) study found the overbite to be averagely the same in the OSAHS (mean 3.73mm, SD 2.03) and the control (mean 3.43mm, SD 1.29), which was insignificant. Battagel and L'Estrange (1996) found the overbite to be normal in the OSAHS (mean 3.4mm, SD 2.5) and the controls (mean 3.6mm, SD 2.2), which also demonstrated insignificant result.

This present study showed overbite to be deeper in the OSAHS group (mean 3.93mm, SD 2.81) when compared to the control (mean 3.47mm, SD 2.1), but statistically insignificant.

Tangugsorn et al., (1995) study found the overjet to be averagely the same in the OSAHS (mean 3.63mm, SD 2.49) and the control (mean 3.71mm, SD 1.96), which was insignificant. Battagel JM and L'Estrange PR, (1996) found the overjet to be normal in the OSAHS (mean 3.4mm, SD 3.0) when compared to the controls (mean 3.0mm, SD 1.6), which also demonstrated insignificant result.

This present study showed reduced overjet in the OSAHS group (mean 3.32mm, SD 2.60) when compared to the control (mean 3.42mm, SD 2.65). The overjet and overbite appeared to be of little or no significance in relation to the severity of the OSAHS condition.

The literature pertaining to the hyoid bone position and its relationship to the sleep apnoea condition is extensive. Bibby RE and Preston CB, (1981) concluded from a review of cephalometric studies of the hyoid that its position generally exhibited 'large' intra- and inter-individual variation. They suggested that this variation could be explained on the basis that most of the reviewed studies had related the hyoid position to the cranial base, rather than more local structures, and that the vertical position of the hyoid relative to the cranial base was strongly influenced by changes in head posture. To overcome limitations of measuring hyoid position relative to distant anatomic structures, they introduced the concept of describing the hyoid position using the 'Hyoid Triangle', which related the hyoid to the most inferior and anterior point on the third cervical vertebra (CV_{3ia}), and the most inferior and posterior point upon the mandibular symphysis (RGN). The horizontal position of the hyoid within this triangle has been consistently reported to be extremely stable throughout life, and this is proposed to be a reflection of the physiological maintenance of upper airway patency (Bibby and

Preston, 1981). It was therefore presumed that the hyoid position in the horizontal plane would be unlikely to exhibit any relationship to OSAHS severity and subsequently the present investigation focused upon vertical relationship between the hyoid and anatomic points and planes.

A lower hyoid position has been frequently reported in OSAHS subjects as compared with 'normal' subjects (Djupestrand et al., 1987; Maltais et al., 1991; Tuchiya et al., 1992; Tangugsorn et al., 1995; Battagel JM and L'Estrange PR, 1996) and non apnoeic snorers (Michizuki et al., 1996; Lowe et al., 1997). A meta-analysis undertaken by Miles et al., (1996), calculated that the mean difference in mandibular plane to hyoid distance between 'normal' and OSAHS subjects was 6.2mm. This difference was significantly greater than the observed 'normal' increase in the same distance of 2.8 with increasing age.

A relationship between NHP, craniofacial structure and hyoid bone position, which also reflects the vertical position of the tongue (Behfelt et al., 1990), has been demonstrated by Tallegran and Solow (1987). Correspondingly, Ozbek et al. (1998), found a higher correlation between a lower hyoid bone position in relation to the mandibular plane and increases in cranio-cervical extension ($P \leq 0.001$). As suggested by Thurow (1977), a low hyoid with a low tongue posture puts the geniohyoid at a mechanical disadvantage by creating a need for tongue elevation, which results in more downward and backward postural forces on the mandible. These, together with a large tongue, may cause an increase in the mandibular load and thereby an interruption of the postural balance of the cranio-mandibular region (Thurow 1977). The increased load on the postural muscles of the mandible (mandibular closing muscle) and the head (post-cervicals) may cause a CCE (cranio-cervical extension).

This present study demonstrates that there is statistically significant result between OSAHS and inferior position of the hyoid bone.

H-H1 (hyoid bone to mandibular plane) found to be more inferiorly positioned in the OSAHS (mean 22.88mm, SD 6.51), than the control (mean 18.58mm, SD 4.72, $P=.002$).

H-H2 (hyoid bone to the plane RGN-Cv3ia) also found to be inferiorly positioned in the OSAHS (mean 12.21mm, SD 6.23), than the control (mean 8.67mm, SD 6.00, and $P=.011$).

(H-H1)+(H-H2) has also found to be inferior in the OSAHS group (mean 35.10mm, SD 11.68,) than the control (mean 26.58mm, SD 9.02), with high statistical significance ($P=.001$).

A Bon Ferroni correction could also be used to achieve the same significance.

Table 7.1 Comparison of Angular measurements with other studies

Variables	Present Study (n=65)			Solow B et al., 1993 (n=50)			Tangugsorn V et al., 1995 (n=100)			Battagel JM and L'Estrange PR 1996 (n=35)			Sakakibara H et al., 1999 (n=60)		
	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.
NSL/OPT	103.82	7.99	.010	104.1	9.09	<.01	106.44	9.03	<.001	-	-	-	109.1	7.8	<.02
FH/OPT	96.54	7.17	.002	95.0	8.75	<.01	98.22	8.62	<.001	-	-	-	103.9	7.3	<.02
NL/OPT	95.85	7.95	.003	96.2	8.89	<.01	97.27	8.77	<.001	-	-	-	100.9	7.4	<.02
NSL/CVT	110.27	7.00	.871	108.0	9.04	<.01	108.96	7.93	<.001	-	-	-	-	-	-
FH/CVT	103.13	6.09	.533	99.0	8.45	<.01	100.73	7.45	<.001	-	-	-	-	-	-
NL/CVT	102.45	7.05	.510	100.4	9.17	<.01	101.79	7.61	<.001	-	-	-	-	-	-
OPT/CVT	6.46	3.17	.000	4.5	2.91	Ns	3.55	2.96	<.001	-	-	-	1.1	2.6	Ns
NL/NSL	8.41	3.60	.605	-	-	-	9.31	3.72	.87	-	-	-	-	-	-
MP/NSL	36.20	6.19	.914	-	-	-	33.56	8.17	<.001	-	-	-	-	-	-
NL/MP	28.34	6.24	.255	-	-	-	-	-	-	26.5	7.9	Ns	-	-	-
FH/NSL	8.25	3.17	.839	-	-	-	8.29	3.07	.01	-	-	-	-	-	-
SNA	82.31	6.46	.023	-	-	-	-	-	-	81.6	3.8	Ns	83.7	4.0	Ns
SNB	79.17	8.09	.336	-	-	-	-	-	-	79.2	4.1	Ns	79.2	4.1	Ns
ANB	4.16	3.78	.877	-	-	-	-	-	-	2.1	2.8	Ns	3.6	2.7	Ns
U1/L1	136.77	12.01	.123	-	-	-	-	-	-	-	-	-	-	-	-
U1/NL	106.46	7.90	.468	-	-	-	-	-	-	110.0	5.1	Ns	-	-	-
L1/MP	88.71	9.06	.061	-	-	-	-	-	-	89.1	7.9	Ns	-	-	-

Table 7.2 Comparison of Linear measurements with other studies

Variables	Present study (n=65)			Lyberg T et al., 1989 (n=25)			Tangugsorn V et al., 1995 (n=100)			Battagel JM and L'Estrange PR 1996 (n=35)			Sakakibara H et al., 1999 (n=60)		
	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.	Mean	SD	Sig.
N-NL	53.95	4.12	Ns	56.4	3	Ns	55.98	3.39	Ns	52.7	3.3	Ns	59.8	4.2	Ns
Gn-NL	68.39	7.4	.000	73.4	5.1	Ns	75.93	6.34	<.001	67.6	7.2	Ns	82.7	5.7	Ns
S-NL	43.6	3.79	Ns	45.2	3.2	Ns	43.91	3.34	<.05	-	-	-	40.8	3.7	Ns
Go-NL	36.2	5.98	0.01	41.8	5.9	Ns	41.37	5.99	<.05	-	-	-	56.7	6.5	Ns
N-S	73.35	4.06	Ns	-	-	-	71.18	3.13	<.001	70	2.6	0.001	71.9	3.8	<.001
ANS-PNS	54.26	4.99	0.001	55.7	3.1	Ns	54.86	3.54	<.01	-	-	-	52.6	5	Ns
Me-Go	73.21	6.55	Ns	77	5.2	Ns	72.85	5.09	Ns	69.7	5.9	0.002	75	5.6	Ns
OB	3.93	2.81	Ns	3.2	2	Ns	3.73	2.03	Ns	3.4	2.5	Ns	-	-	-
OJ	3.32	2.6	Ns	2.5	2.3	.000	3.63	2.49	Ns	3.4	3	Ns	-	-	-
H-H1	22.88	6.51	0.002	26.9	6.5	<.001	25.36	5.72	<.001	25.9	4.8	Ns	23.2	6.9	<.001
H-H2	12.22	6.23	0.011	-	-	-	-	-	-	-	-	-	-	-	-
(H-H1)+(H-H2)	35.1	11.68	0.001	-	-	-	-	-	-	-	-	-	-	-	-

CONCLUSION

The value of the cephalometric radiograph in the study of the head and neck is a valuable tool in the evaluation of OSAHS patients, giving important information relating to the hard and soft tissue morphology of the cranio-cervico-facial complex, and guidance towards a rational treatment modality. It is widely accessible and relatively inexpensive in comparison to alternative imaging procedures.

Our results indicate that there are significant cranio-cervico-facial differences between OSAHS group and the control.

These differences could be summarized as follows:-

1. Increased cranio-cervical angulations (NSL/OPT), (FH/OPT), (NL/OPT), (NSL/CVT), (FH/CVT) and (NL/CVT).
2. Decreased cervical curvature (CVT/OPT), which shows further forward positioning of the head.
3. Minimally decreased maxillary inclination.
4. Minimally decreased mandibular inclination.
5. Increased maxillary mandibular plane angle.
6. Clockwise rotation of the craniofacial complex.
7. An increased tendency for CL II skeletal cases suffer from OSAHS when compared to CL III (Increased SNA, SNB, and ANB).

8. The relationship between the maxilla and the mandible (increased MMP angle, decreased U1/NL and L1/MP and increased U1/L1), can lead to downward and backward rotation of the maxillary / mandibular complex.
9. A minimally longer upper anterior facial height (N-NL) and a significantly longer lower anterior facial height (Gn-NL).
10. A longer upper (S-NL) and lower (Go-NL) posterior facial height.
11. A shorter anterior cranial base length (S-N).
12. A shorter maxillary length (ANS-PNS).
13. A shorter mandibular length (Me-Go).
14. Deeper overbite (OB).
15. Minimally reduced overjet (OJ).
16. Inferiorly positioned hyoid bone, increased length of (H-H1), (H-H2) and (H-H1) + (H-H2).

The 'null hypothesis' as follows:

- I. The craniofacial morphology and the position of the hyoid bone in relation to the cervical vertebrae and / or a fixed point upon the anterior cranial base, provides no indication to the severity of OSAHS. This statement found to be false.
- II. There are no significant differences in skeletal morphology between the OSAHS group and the controls matched for sex, age and ethnicity. This is also found to be false.

Orthodontists may therefore find themselves in a position to assist in the early identification of patients with OSAHS. The ready availability of the lateral

cephalograms may help to identify the patient at risk who can then be referred for further investigation. In addition, treatment options for the subject with OSAHS may involve the provision of mandibular advancement splints. The orthodontist is uniquely placed to provide these appliances. Finally, where maxillo-facial surgery is recommended, the orthodontist will be involved in the pre-surgical co-ordination of the occlusion. The limitations will be in the younger age group in the orthodontic population, as most of the OSAHS patients are above 40 years of age. To overcome this problem, there should be a close relationship between an ENT, a neurologist, a cardio-respiratory specialist, maxillo-facial surgeon, orthodontist and a sleep laboratory.

I recommend further studies in the use of lateral cephalometric radiograph analysis of the hard (cranio-cervico-facial morphology and hyoid bone position) and soft tissues (pharyngeal width, tongue and soft palate length) using different cephalometric analysis to further aid in the diagnosis and treatment of OSAHS.

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APPENDIX

- Angular measurements (Subjects n=65)
- Angular measurements (Control n=30)
- Linear measurements (Subjects n=65)
- Linear measurements (Control n=30)

Angular measurements (Subjects n=65)

Subjects	NSL/OPT	FH/OPT	NL/OPT	NSL/CVT	FH/CVT	NL/CVT	CVT/OPT	NL/NSL	MP/NSL	NL/MP	FH/NSL	SNA	SNB	ANB	U1/L1	U1/NL	L1/MP
1	106	108	96	110	112	100	4	11	35	24	16	85	80	5	169	90	76
2	112	102	108	115	105	111	3	5	39	34	12	80	82	3	149	96	80
3	105	94.5	100	109	98.5	104	4	7	31	26	10	88	82.5	5.5	147	103.5	84
4	106	94	98	109	97	101	3	9	40	32	13	83	75	8	140	107	82
5	101.5	91	95	107.5	97	101	6	7	40	33	10	90	79	11	115	111	100
6	106.5	102	103	109.5	105	106	3	3	29	25.5	5	78	77	2	157	106	72
7	95	92.5	90	100	97.5	95	5	5	34	29	4	82	77	5	113	108	111
8	100	92.5	92.5	112	104.5	104.5	12	7	36	28	8	83	79	4	140	109	83
9	100	91	89	108	99	97	8	12	31	19	9	82	81	1	126	124	92
10	96	89	91	103	96	98	7	6	37	33	8	81.5	76.5	5	113	106	87
11	119	103	105	123	107	109	4	14	43	29.5	16	74	72.5	1.5	138	111	82
12	125	112	108	134	121	117	9	17	39	22	14	78.5	73	5.5	127	108	102
13	105	97	95.5	115	107	105.5	10	9	41	30.5	9	82	74.5	7.5	130	104	97
14	101	97	94	107	103	100	6	7	42.5	36	4	84	78	6	118	110	95
15	103	101	99	114	112	110	11	4	34	31	4	76.5	75.5	1	138	102	99
16	115	98	105.5	120	113	110.5	5	10	39.5	30	8	79.5	74.5	5	160	95	75
17	105	99	100	115	109	110	10	4.5	31	26	6	84.5	82	1.5	113	119	102
18	93	91	87	100	98	94	7	7	34	27.5	3.5	86	79	7	129	110	96
19	96	88	95	103	95	102	7	3.5	39	39	8.5	103.5	98	5.5	122	104	96
20	108	95	103	117	104	112	9	5	38	32	13	81	78	3	138	106	93
21	116	110	110	119	113	113	3	7	39.5	33	7	114	113	1	152	92	83
22	106	98	94	114	106	112	8	4.5	35	32	8	80	82	-2	120	112	95
23	105	97	91	112	103	98	7	13.5	26	13	13	78	76	2	138	117	93
24	98	91	94	107	100	103	9	4.5	33	29	8	83	81.5	1.5	127	110.5	93.5
25	92	92.5	92	101	101.5	101	9	10	37.5	27	9.5	78	73	5	135	101	94
26	116.5	105.5	105.5	120.5	109	109.5	4	11.5	37	27	11	74	69.5	4.5	167	84	82
27	108	97	103	115	104	110	7	6	38	32	11	79	76	3	132.5	110	85
28	104	95	97	108	99	101	4	8	36	29.5	10	87	78	9	140	102	89
29	92	83	89	106	97	103	14	4	32	29.5	9	78	74.5	3.5	135	97	98
30	93	80	90	105	92	102	12	4	37	32.5	13	80	77.5	2.5	141	100	96
31	120	110	112.5	122.5	112.5	115	2.5	8.5	43.5	36	10	81	71	10	152	90	82
32	104	95.5	94	109	100.5	99	5	8	23	12.5	10	83.5	82.5	1	151	106	90
33	105	92	94	112	99	101	7	11	43	32	13	85	76	9	118	113	98

Angular measurements (Subjects n=65)

Subjects	NSL/OPT	FH/OPT	NL/OPT	NSL/CVT	FH/CVT	NL/CVT	CVT/OPT	NL/NSL	MP/NSL	NL/MP	FH/NSL	SNA	SNB	ANB	U1/L1	U1/NL	L1MP
34	124	113	118.5	126	115	120.5	2	5	41	36	12	75	76	-1	151	101	72
35	103	96	88	114	107	99	11	15	43.5	38.5	6.5	85	77	8	138	114	80
36	110	104	104	113	107	107	3	6	33	27	7	85	77	8	122	112	79
37	101	97	97	107	103	94	6	13	32	28.5	4	83	78	5	144	106	91
38	105	98	98	109	102	103.5	4	6	23.5	18	7	81	81	0	148	110	85
39	99	91	91	107	99	99	8	7.5	32	25	7	84	75.5	8.5	129	98	109
40	98.5	94	90	102.5	98	94	4	9	26.5	17.5	5	86.5	81.5	5	160	97	85
41	93	85	77.5	99	91	83.5	6	16	45	29	9	81.5	74.5	7	119	116	96
42	112	102.5	96	117	107.5	101	5	16	48	31	9	75	70	5	122	91	84
43	99	95	87.5	108	104	96.5	9	12	31	19	4	83	79	4	138	111	91
44	104	98	90.5	108.5	102.5	95	4.5	14	40	27	6	77	75	2	125	116	92
45	101	99	95	105	103	99	4	5	28	22	3	91	87	4	132	119	88
46	105	96	96	107	98	98	2	8	34	25	8	80	75	5	125	113	97
47	94	92.5	91	96.5	95	93.5	2.5	4	25	22	3	89	83	6	141	108	89
48	95	84.5	83.5	110.5	100	99	15.5	12	37	25	11	74.5	73	1	136	110	89
49	108.5	109	105.5	113.5	114	110.5	5	3.5	33	30	3.5	82	80	2	158	97	74
50	112	104.5	103	116.5	109	107.5	4.5	9.5	49	40	8	82	74.5	7.5	117	118	94
51	96.5	95.5	101	106.5	105.5	111	10	5	45	40	11	81	75	6	140	100	79
52	108	101	103	111	104.5	106	3	5	33	28.5	6.5	82.5	78.5	5	141	105	86
53	101.5	97.5	90	103.5	99.5	92	2	12	41	29	5	78	75	3	133	112	86
54	98	88.5	85	106	96.5	93	8	12.5	48.5	36.5	9	97	74	23	120	113	91
55	102.5	101.5	102.5	105.5	104.5	98	3	7	29	22	3	84.5	83.5	-1	152	108	77
56	98	90.5	98	107.5	100	98.5	9.5	9.5	28.5	19	8	80	82	-2	147	110	84
57	84	80.5	84	95.5	92	87.5	12.5	8.5	38	30	4.5	77.5	76	1.5	140	111	78
58	98.5	91	98.5	103.5	96	99	5	4.5	39	25	8	78	77	1	137	106	92
59	113	105	113	118	110	108	5	10	41	31	8	79.5	75.5	4	129	108	92
60	104	97	104	112	105	102.5	8	10	43	34	7.5	78	74.5	3.5	139	107	100
61	113	103.5	113	118	108.5	107.5	5	10.5	29	18	10	79	76	3	137	105	100
62	102	95	102	107	100	101.5	5	5	37	32	7	80.5	76	3.5	135	114	80
63	96.5	90	96.5	109	102.5	97.5	12.5	12	37	35	7	75.5	75	0.5	172	96	66
64	104	94.5	104	110.5	101	97	6.5	12.5	44	31	9.5	77.5	75.5	2	135.5	108	85.5
65	107	101	107	112	106	105	5	7.5	25	18	6	84.5	83	1.5	137	113	93

Angular measurements (Control n=30)

Control	NS/OPT	FH/OPT	NL/OPT	NS/LCVT	FH/LCVT	NL/LCVT	CVT/OPT	NL/NSL	MP/NSL	NL/MP	FH/NSL	SNA	SNB	ANB	U1/L1	U1/NL	L1/MP
1	99.5	95.5	92.5	105.5	101.5	98.5	6	7.5	33	26	4.5	84	78.5	5.5	115	119	101.5
2	98	87	89	103.5	92.5	94.5	5.5	9	37	29	10.5	88	78.5	9.5	120	117	99
3	110	103.5	101.5	114	107.5	105	4	9	34.5	25.5	7	77	75	2	130	106	96
4	99	98	92.5	105	104	98.5	6	7	23.5	16.5	2.5	85	80	5	118	114	111
5	93	89	84	104	100	95	11	9	52.5	44	4.5	82	70	12	151	78.5	77
6	92	88	90	108	104	106	16	4	40	37	4	75	80	-5	141	107	75
7	95	90	87.5	102	97	94.5	7	7	39	31	5	81.5	79.5	2	128.5	114.5	86
8	110.5	100	96	123.5	113	109	13	15	36	23	11	77	74	3	140	104	86
9	103.5	88.5	96	110	95	102.5	6.5	7.5	41	33.5	15	87	72.5	14.5	132	104	91.5
10	113	106.5	103	123	116.5	113	10	10	41	31	7	79	76	3	114	115	100
11	75	73.5	67.5	94	92.5	86.5	19	7.5	35	27.5	2	79	80	-1	130	119	104
12	108	105.5	100	119	116.5	111	11	7.5	30	23	2	84	80	4	152.5	100	84
13	100.5	87.5	92.5	112.5	99.5	104.5	12	8.5	30.5	22.5	14	82.5	81	1.5	130	110	94
14	84	79	76.5	100	95	92.5	16	7.5	25.5	18	4.5	78	73.5	4.5	120	119	104
15	100.5	92.5	92	106.5	98.5	98	6	8	33	25	8	85	80	5	101.5	125.5	108
16	95	85.5	82.5	103.5	94	91	8.5	12.5	46	34	9	77	75	2	141	105	80
17	88	76	80	98	86	90	10	8	34	26.5	11.5	81	75	6	142	96	95
18	96	90	88	109	103	101	13	8	34	25	5	85	80	5	139	103	92
19	106	100.5	96	110.5	105	100.5	4.5	5	40	3	10	82	82	0	132.5	108	88.5
20	94	82	88	104	92	98	10	7	27	22	12	86	80	6	118	114	106
21	101.5	91.5	88.5	124	114	111	22.5	14	45	30	11	78	71	7	132	110	87
22	93	85	82	102	94	91	9	10.5	33	23	8	80	77	3	134	111.5	90.5
23	93	89	87	113.5	109.5	107.5	20.5	7	28.5	22	4.5	84.5	83	1.5	135	111	91
24	91	83	86	98.5	90.5	93.5	7.5	8	37	21	9.5	85	83	2	137	107	84
25	107.5	94	97	121	107.5	110.5	13.5	10.5	43	32	13	73	71	2	136	102	90
26	107	94	96	122	109	111	15	11	39.5	28	13	80	76	4	129.5	111	91
27	108	94	96	116	102	104	8	12.5	42	31	14	77	74	3	139	106	86
28	110	107	101	117	114	108	7	10	40	30	3	80	73	6.5	158	95	84
29	96	86	89	114	104	107	18	8	31	23.5	10	77.5	75.5	2	130	105	101
30	104.5	96	97	116.5	108	109	12	7.5	39	31	8	78.5	73.5	5.5	138	97	92.5

Linear measurements (Subjects n=65)

Subjects	N-NL	Gn-NL	S-NL	Go-NL	N-S	ANS-PNS	Me-Go	OB	OJ	H-H1	H-H2	(H-H1)+(H-H2)
1	51.5	62.5	39	35	65.5	44.5	64.5	5	2	18	9.5	27.5
2	44	61	39	27	64.5	37.5	62	4.5	-2.5	11	6	17
3	50	63	44	34.5	70	47	69.5	4	2.5	28	16	44
4	54	64.5	44	29	70	52	69	2	4	27	16.5	43.5
5	54.5	74.5	46	39.5	73	59	62.5	3	5	27	16	43
6	48	63	44	35	73.5	48	71	10	7	33	13	46
7	53	70	46	39	75	56	62	2	3	18	10.5	28.5
8	54	72	44.5	37	73	51	73	5	5	17	3	20
9	56	61	42	39.5	71.5	56	72	2	2	11.5	5	16.5
10	52	79	46	41	76.5	58	70	-7	2	18	12	30
11	54	60.5	38.5	29	64	53	66	5	5	25	5.5	30.5
12	57	64	32	40	69.5	54.5	68	2	2	15	11	26
13	54	68.5	41	35	77.5	52.5	67.5	9	5.5	31	18.5	49.5
14	51	64	43	25	70	58	68.5	2	2	17	10	27
15	47.5	66	44.5	34	72	48.5	65	0	0	27	10.5	37.5
16	56	69	45.5	35.5	67	47	68	2.5	1	26.5	12	38.5
17	48	68.5	42	38.5	69	49.5	69	2.5	2	12.5	2	14.5
18	51	63	43	33.5	69	55	65	6	7	21	12.5	33.5
19	46	69	45.5	27	68	51	69	3.5	5	15	6	21
20	53	67	47	30	73	52	72	6	5	27	12	39
21	54	71	46	32.5	72.5	49	75.5	5.5	1	16	3	19
22	51	69	49	29.5	73	52	65	4	3.5	23	3.5	26.5
23	59	56	40.5	39.5	78.5	58	73	5	4	17.5	9.5	27
24	50	69	45	33	72	54	75.5	4	2	24	13	37
25	53	64	41	36	69	52	69	6.5	4	24.5	21	45.5
26	52	60	39	34.5	74	42.5	64	9	1.5	20	3.5	23.5
27	50	77	43	30.5	74	53	70	6	5	20	7.5	27.5
28	46	68.5	37.5	30	71	55	71.5	7	3	23	13	36
29	49	57	45	35.5	72	51	67	5	3.5	33	17.5	40.5
30	53	82	47.5	43.5	81.5	59	77	4	3	21	10	31
31	52	62	43	23	68	47	64.5	6.5	6	26	4	30
32	47.5	53.5	35.5	40.5	71	50	72	2	-2	22	10.5	32.5
33	59	72	45	34.5	73	61	72	4	4	27	16.5	43.5

Linear measurements (Subjects n=65)

Subjects	N-NL	Gn-NL	S-NL	Go-NL	N-S	ANS-PNS	Me-Go	OB	OJ	H-H1	H-H2	(H-H1)+(H-H2)
34	54	73	47	31	72.5	58	66	0	0	31.5	12	43.5
35	59	60	40	25	71	60	80	4	5	37	23	60
36	55.5	74	48	41.5	73.5	61.5	74	10	10	28	25.5	53.5
37	59	65	42	42	74	59	74	3.5	3	30	23	53
38	56	66	48	44	74	53	88	4.5	3	30.5	21	51.5
39	53	72.5	43	38	80	61	882	4	4	12	6.5	18.5
40	57	55	46	36	72	58	72	3	3	21	14	35
41	56.5	65.5	36	31	74	51	76	5.5	5	14	2	16
42	61.5	76	40	41	76	57	74	6	2	28	15	43
43	59	71	39.5	48	75	59	79	3	3	33	24	57
44	61	71	44	36	76	58.5	85	3.5	3	11	5	16
45	55	70	47	41.5	78.5	64	89	4	3	19	13.5	32.5
46	57	71	44	40	83	62	80	4	4	29	26	55
47	51	67	47.5	40	75	61	80	7	2	9.5	9	18.5
48	57.5	67.5	43	40	69	50	70	1	2	17.5	13	30.5
49	58	77	53	39	79.5	58	80	3	1	29.5	18.5	48
50	58	82.5	46	39.5	78	59	79	0	2	33	12	35
51	50	72	45	25	70	50	74	6	7	29	14	43
52	47.5	77	41.5	43.5	77	57	74	6	3	19	11	30
53	61	77	45	41	78.5	57	78	2	2	21	11	33
54	55	69	39	31	70.5	55	69	4	3	23	16.5	39.5
55	55	72.5	45	42.5	77	54.5	82	-2	1	19.5	7	26.5
56	52	73	41	48	75	52	82	0	1	19	12.5	31.5
57	57.5	82	47	43	78	59	85	2.5	6.5	31	26.5	57.5
58	55.5	69.5	50	37	77.5	58	83	4.5	4	24.5	20	44.5
59	59.5	73	47.5	39	79	56	80	4	1.5	29	8	37
60	55	69.5	41.5	30	77	54	81	2	3	21	6	27
61	58	65	44	44	75	55	73	5	3.5	22	11.5	33.5
62	49.5	67	48.5	27	69	52	79	2	2	22	5	27
63	55	62	40	32	73	53	73	10	1.5	30	19	49
64	59	82	41.5	44.5	78	56	77	2	2	18	10	28
65	59	65	50	45	71	55	71	4	2.5	23	12.5	35.5

Linear measurements (Control n=30)

Control	N-NL	Gn-NL	S-NL	Go-NL	N-S	ANS-PNS	Me-Go	OB	OJ	H-H1	H-H2	(H-H1)+(H-H2)
1	55	62	46	35	75.5	61	77	3	3	18	11	29
2	51.5	59	41.5	27	69	60	74	3	3	16	10	26
3	54	56	43	28	73	62.5	78	5	5	20	10	30
4	50	53	41.5	34	76.5	58.5	77.5	4	3	16	4	20
5	57	69	46	24.5	74	58	77.5	9	2	19	13	32
6	54	77	51	30	75.5	59	83	-2	1	23.5	16	39.5
7	51	69	42	27.5	77	59.5	85	3	3	20.5	16	36.5
8	57	62	37	37	78	56	85	5	2	18.5	3	21.5
9	53	62.5	44	26	71	60.5	72	2	13	8	-3	5
10	50	65	37	35	70	58	67	2	3	22.5	9	31.5
11	55.5	69	46	35	75	62.5	80	3	2	27	26	53
12	50	61	40.5	35	71	57	76	2	3.5	18.5	3	21.5
13	53	54.5	43	30	71	54	79	2.5	2	13	4	17
14	53	59	44	40	73	60.5	69	4.5	8	13	9	22
15	56	66	45	35	74	59	78	4	6	12	3	15
16	55	65	39	30	73.5	50	67	2.5	2	15	6.5	21.5
17	54	62	44.5	34.5	72.5	55	66.5	4	2	11.5	6	17.5
18	53	62	42	34	77	56	76	5	2	19	7.5	26.5
19	52	65	41	33.5	66.5	59	66	-1	-2	23	10	33
20	49	55	41	32	72	53	69	4	5	16	8	24
21	56	67	39	35	78	56	67	3.5	7	27.5	13.5	41
22	57	64	42.5	36	76	58	78	5	4	21	10.5	31.5
23	61	67	53	44	77	61	78.5	2	4	21	14	35
24	56	62	47.5	40.5	78	59	70	6	2	24	18	42
25	53	57	40	23	70	50	70	4	2	18	2	20
26	55	61	41.5	31.5	73	59	73	6	4	16	3	19
27	54.5	58	41	27	67.5	53	74.5	5	3	21	7	28
28	52.5	57	41.5	30	68	53	65	5	5	19	4	23
29	54	64	44	41	76.5	61	78	1	1	14	2	16
30	50	68	41	32.5	73.5	58.5	75	2	2	26	14	40